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CARDIOSPASM AND ESOPHAGITIS: AN EXPERIMENTAL STUDY OF THE ESOPHAGOGASTRIC SPHINCTER*

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As is so often the case when the etiology of a condition is unknown, the methods of treatment are not only multifarious but are quite unsatisfactory as well. Certainly cardiospasm, falling easily into that category, has stimulated the therapeutists to unique and sometimes clever gadgetry to salve the horror of starvation. The first recorded treatment, eminently successful in preserving life although failing to relieve the spasm, was poignantly described in 1674 by Thomas Willis.[18] He devised the whalebone tamponade with which, for over 15 years, the patient self-administered his masticated food (fig. 1). At the present time modern medical science can boast of a number of medical and surgical advances in the treatment of achalasia, yet the step-child of the whalebone tamponade, the esophageal bougie, continues to provide good palliation for a good share of patients.

For other patients with severe cardiospasm, treatment by surgery has yielded another fair share of benefit, but the now recognizable complication of esophagitis becomes a deterrent to universal treatment of cardiospasm by present surgical means. Any treatment which relieves the obstruction caused by the "*spasm*" of the lower esophagus and thus necessarily abridges the function of the valve or sphincter between esophagus and stomach leads to a situation which allows reflux into the esophagus.

Considering the fact that cardiospasm is second in frequency to carcinoma in causing symptoms of esophageal obstruction,[15] it is surprising that so little is known of its etiology and abnormal physiology. The clinical features of the disease are attributable to the spastic contraction of the cardiac portion of the

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esophagus. There is no anatomic stenosis but there is more or less dilatation of the esophagus above the point of obstruction. The cardinal symptoms are epigastric or retrosternal pain, dysphagia, and regurgitation. Frequently pulmonary symptoms result from aspiration of regurgitated material. The disease may begin either gradually or suddenly and may occur at any time of life in either sex. Cardiospasm must be differentiated from carcinoma, benign stricture, hiatus hernia, esophagitis, varices, benign tumor, or diverticula. In infants, cardiospasm (achalasia) should not be confused with chalasia of the esophagus in which instance the esophagogastric junction is widely patulous. A barium meal usually is diagnostic of any of these abnormalities although esophagoscopy is valuable and essential in difficult cases.

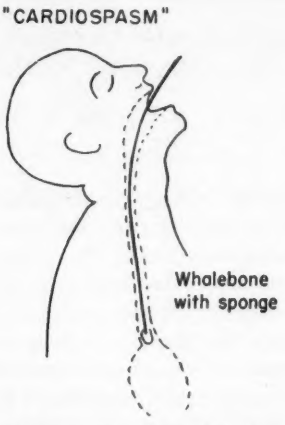

FIG. 1. Diagram illustrating an early method of treatment for cardiospasm by Thomas Willis in 1674. A whalebone with a sponge was used by the patient to force the food into the stomach for sustenance.

Cardiospasm resembles Hirschsprung's disease (congenital megacolon) in some respects but the evidence of similarity is not conclusive. There apparently is a neuromuscular imbalance in that the cardia fails to relax when a peristaltic wave reaches it. Abnormalities of the ganglion cells of the myenteric plexus have been described. Lendrum[10] reported his studies of the myenteric layer of 13 autopsied cases of cardiospasm and 58 cases of the normal adult esophagus. There was a striking decrease in the number of ganglion cells in the cardiospasm cases as contrasted to the normal. The ganglion cells were decreased in number in both the dilated esophagus and the undilated terminal esophagus. There was no anatomic sphincter nor organic stricture in any patient. Others have noted similar changes in the myenteric layer of the esophagus.[12] Dornhorst[6] has measured the intraesophageal and the intragastric pressures in patients with cardiospasm.

The surgical treatment of cardiospasm, when bouginage fails, has been directed to incision, revision, excision, or by-passing of the esophagogastric junction

(fig. 2). The Heller operation, claiming many proponents, consists of incising longitudinally the muscular layers of the esophagus and stomach down to, but not through, the mucosa. Good results have been claimed by several authors.[1, 14] However, esophagitis may occur following this operation in patients and in experimental dogs.[8] The Gröndahl operation, or esophagogastrostomy, having had some support,[11] also is attended by the complication of reflux esophagitis.[2, 8] Anastomotic procedures between the esophagus and stomach, by-passing the junction or after excision of the junction, for cardiospasm or carcinoma, also are beset with a rather high incidence of esophagitis.[2, 13] In an attempt to decrease the reflux of acid into the esophagus after excision of the cardia and lower esophagus for cardiospasm, extensive gastric resection with Ramstedt type of pylorotomy was added to the excision.[16] It has been learned that reflux of alkaline material also produces esophageal erosion.[3] Surgically-fashioned valves have been devised in the surgery for cardiospasm.[4, 17] Recently interposition of a jejunal segment between the esophagus and the stomach after excision of the junction has been carried out[5] (fig. 3). The jejunum has been shown to be less sensitive to erosion and ulceration than the esophagus.[9] It remains to be shown conclusively whether such an interposed segment acts merely as a conduit or as a functioning sphincter in protecting the sensitive esophageal mucosa.

It might be expected that vagus section would be beneficial to patients with esophagitis complicating the treatment of cardiospasm due to its effect in diminishing gastric secretions; however, vagotomy does not protect against such an occurrence in patients[16] nor in experimental animals.[8]

In view of the suggested physiologic abnormality of the esophagogastric junction in cardiospasm, and the many surgical procedures for ablation of the

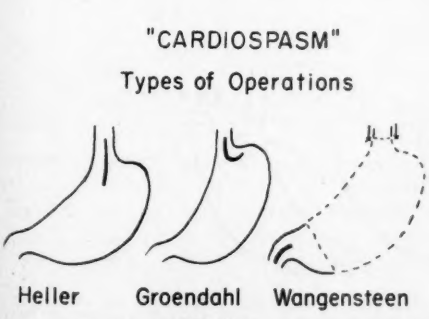

FIG. 2.

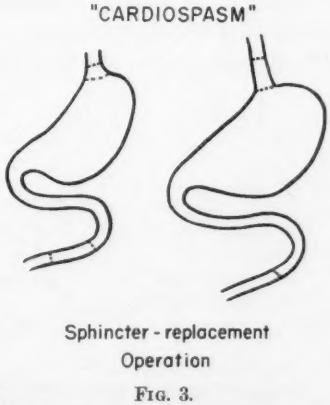

FIG. 3.

FIG. 2. Diagrammatic illustration of some types of operations done for cardiospasm. The Heller operation is an incisional type (to mucosa); the Gröndahl operation is an anastomotic revision type; and the Wangensteen operation is an excisional type with added subtotal gastrectomy, vagotomy and pyloromyotomy.

FIG. 3. Diagrammatic illustration of a sphincter-replacement operation for cardiospasm in which a segment of jejunum is interposed between the esophagus and stomach after excision of the esophagogastric junction.

area, we have done certain experiments to obtain information regarding the function of the esophagogastric junction of the dog.

METHOD OF EXPERIMENTATION

Adult mongrel dogs were used throughout the experiments, in several series. All dogs had esophagogastrostomy as an anastomotic by-pass of the cardio-esophageal junction and observations of the esophagus just above the anastomosis as well as above the junction were recorded. In two series vagotomy, with and without pyloromyotomy, were added to the experimental preparations. Finally some dogs from all series were reoperated upon and esophageal continuity above the junction was reconstructed for later observations.

All operations were done using aseptic precautions and with sodium pentobarbital anesthesia (15 mg. per pound body weight intravenously). The left transthoracic approach was used in each instance, with endotracheal oxygen administration. Hemostatic ligatures and anastomotic sutures were of fine black silk. Parenteral fluids and antibiotics were used postoperatively until food and fluids were tolerated. Gastric analyses following histamine stimulation (and occasionally insulin administration) were obtained before and after surgical operation. The dogs were weighed at regular intervals. Animals were killed under anesthesia. Gross and microscopic examinations of tissues, particularly the esophagus, were made.

Series I. In 9 dogs the thoracic esophagus was divided 3 cm. above the diaphragm. The distal segment was inverted and the proximal segment was anastomosed to the fundus of the stomach which was drawn through an incision in the dome of the diaphragm. Esophagogastric continuity thus by-passes the sphincter (fig. 4).

Series II. In 10 dogs esophagogastrostomy was done as in Series I, with the addition of transthoracic section of the vagus trunks and fibers at the level of the division of the esophagus (fig. 4).

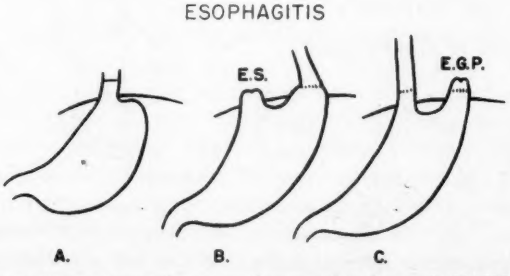

FIG. 4. Diagram of experimental preparations used in Series I, II, III, and IV. A. The line of transection of the esophagus is indicated. B. Series I. Esophagogastrostomy with closure of distal esophageal stump. Series II. Esophagogastrostomy with vagotomy. Series III. Esophagogastrostomy with vagotomy and pyloromyotomy. C. Series IV. The esophagus above the esophagogastrostomy is transected and reanastomosis is done to the esophageal stump (E.S.) over the sphincter with closure of the esophagogastric pouch (E.G.P.)

Series III. In 7 dogs, esophagogastrostomy was done with the addition of vagotomy and pyloromyotomy. (One dog, No. 65, had gastrojejunostomy instead of pyloromyotomy) (fig. 4).

Series IV. Ten dogs from the series I, II, and III were reoperated upon, at which time the condition of the two segments of the esophagus was recorded. At this time the esophagus was divided 3 cm. above the anastomosis. The segment distal to this transection was inverted above the anastomosis while the proximal segment was anastomosed to the esophageal stump (its original position) above the sphincter (fig. 4). The area marked *"EGP"* in figure 4 will be referred to as the esophagogastric pouch and the area marked *"ES"* will be called the esophageal stump.

RESULTS

Series I (Table I). Eight of the 9 dogs with esophagogastrostomy lived longer than 14 days and at reoperation or death demonstrated mild to moderate esophagitis above the esophagogastrostomy. The esophageal stump above the sphincter did not develop esophagitis (fig. 5). In the 1 dog (No. 119), which died in 14 days of empyema due to operative contamination, the esophagus above the anastomosis was normal. One dog (No. 120), with high values of gastric acidity, developed severe esophagitis above the anastomosis with perforation and death in 20 days. On the other hand, dog No. 43, with low gastric acidity, had developed only mild esophagitis above the anastomosis at the time of reoperation in 64 days.

Series II (Table II). Nine of the 10 dogs with esophagogastrostomy and vagotomy developed esophagitis above the anastomosis as observed at autopsy or reoperation. There was one perforated esophagus with death in only 7 days

TABLE I

Series I: Dogs with esophagogastrostomy

Dog No.	Gastric Acidity (Degrees free HCl)	Days	Findings at Reoperation or Autopsy		Remarks
			Esophageal Stump	Esophagus above Anastomosis	
119	60	14	Normal	No esophagitis	Died of empyema due to surgical contamination
120	100	20	Normal	Severe esophagitis with perforation	Vomiting, weight loss
115	—	29	Normal	Moderate esophagitis	Vomiting, weight loss
43	12	64	Normal	Mild esophagitis	Occasional vomiting
47	74	65	Normal	Moderate esophagitis	Slight anastomotic stenosis
114	70	76	Normal	Moderate esophagitis	Occasional vomiting
118	24	77	Normal	Moderate esophagitis	Occasional vomiting
113	0 (no hist.)	78	Normal	Moderate esophagitis	Moderate anastomotic stenosis
117	55	82	Normal	Moderate esophagitis	Occasional vomiting

FIG. 5. Photograph of specimen of stomach and esophagus of dog no. 115 (Series I). The esophagus above the esophagogastrostomy (at the left) shows esophagitis. The esophageal stump (on the right), protected by the sphincter, is normal.

TABLE II

Series II: Dogs with esophagogastrostomy with vagotomy

Dog No.	Gastric Acidity (Degrees free HCl)	Days	Findings at Re-operation or Autopsy		Remarks
			Esophageal Stump	Esophagus above Anastomosis	
91	54	7	Normal	Esophagitis with perforation	Gastric dilatation
80	59	17	Normal	Normal	Gastric dilatation; vomiting
108	24	19	Normal	Esophagitis with bleeding erosions	Esophageal dilatation; vomiting
111	72	20	Normal	Mild esophagitis	Vomiting
126	40	20	Normal	Minimal esophagitis	Gastric dilatation; vomiting
50	82	20	Normal	Minimal esophagitis	Gastric dilatation; vomiting
35	100	20	Normal	Esophagitis with linear ulceration	Gastric dilatation; vomiting
44	25	29	Normal	Esophagitis with erosion	Gastric dilatation; vomiting
139	83	36	Normal	Esophageal ulceration	Gastric dilatation; anorexia
82	115	64	Normal	Mild esophagitis	Infrequent vomiting; gastric dilatation. Reoperated

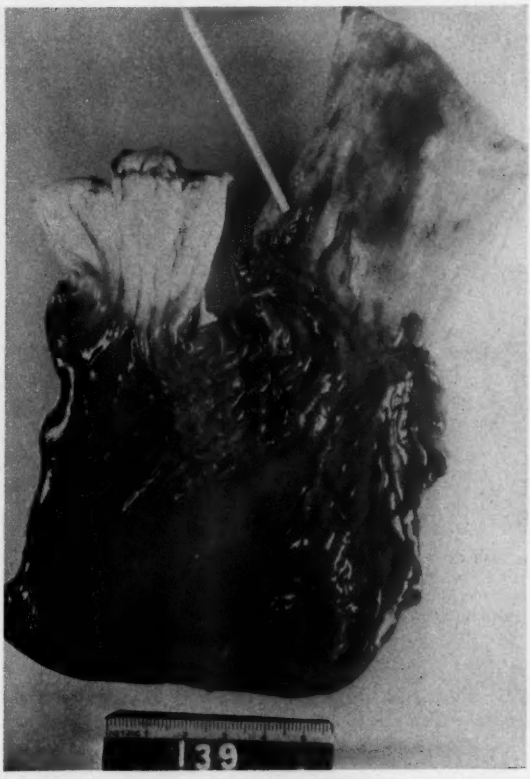

FIG. 6. Photograph of specimen of stomach and esophagus of dog no. 139 (Series II). The distal esophageal stump (on the left) above the sphincter is normal, while the esophagus above the esophagogastrostomy shows severe esophagitis. The pointer indicates ulceration. Vagotomy failed to protect against ulceration of the esophagus.

TABLE III

Series III: Dogs with esophagogastrostomy with vagotomy and pyloromyotomy (or gastroenterostomy)

Dog No.	Gastric Acidity (Degrees free HCl)	Days	Findings at Reoperation or Autopsy		Remarks
			Esophageal Stump	Esophagus above Anastomosis	
65	82	16	Normal	Esophagitis	Jejunal ulcer at gastroenterostomy
59	110	25	Normal	Mild esophagitis	Persistent vomiting
64	80	33	Normal	Esophagitis with large ulcerations	Vomiting
48	30	57	Normal	Moderate esophagitis	Occasional vomiting
112	110	63	Normal	Moderate esophagitis	Esophageal dilatation; vomiting
38	0	63	Normal	No esophagitis	Vomiting
95	30	66	Normal	Moderate esophagitis	Vomiting

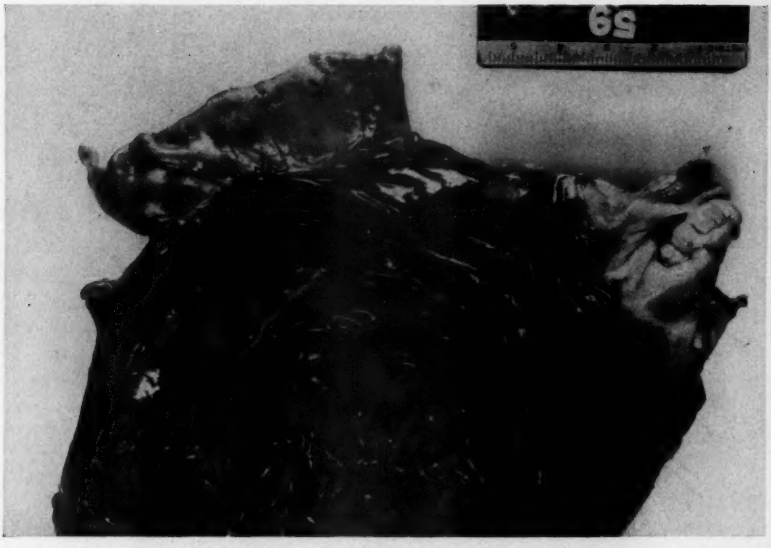

FIG. 7. Photograph of specimen of stomach and esophagus of dog no. 59 (Series III) There is esophagitis above the esophagogastrostomy (on the left) while the distal esophageal stump (on the right) is normal. Vagotomy and pyloromyotomy was done in this dog together with the esophagogastrostomy.

TABLE IV

Series IV: Dogs from series I, II, and III in which the esophagus was reanastomosed to the esophageal stump above the esophagogastric sphincter (see figure 4)

Dog No.	Gastric Acidity (Degrees free HCl)	Days		Original Findings at Reoperation		Fina Findings at Autopsy	
		Re-operation	Autopsy	Esophageal stump (E.S.)	Esophagus above original anastomosis	Esophagus reanastomosed above sphincter	Esophagus at esophagogastric pouch (E.G.P.)
43	12	64	125	Normal	Esophagitis	Normal	Esophagitis with scarring
47	74	65	116	Normal	Esophagitis	Normal	Esophagitis with erosion
114	70	76	84	Normal	Esophagitis	Normal	Esophagitis with ulceration & perforation
118	24	77	149	Normal	Esophagitis	Normal	Esophagitis with ulceration
113	0 (no hist.)	78	121	Normal	Esophagitis	Normal	Moderate esophagitis
117	55	82	144	Normal	Esophagitis	Normal	Severe esophagitis with ulceration
82	115	64	106	Normal	Esophagitis	Normal	Esophagitis with ulceration
48	30	57	127	Normal	Esophagitis	Normal	Esophagitis with ulceration
112	110	63	63	Normal	Esophagitis	Esophagitis	Esophagitis
38	0	63	123	Normal	Normal	Normal	Normal

following operation (dog No. 91). The esophageal stump above the sphincter was normal in every instance (fig. 6). One of the 10 dogs (No. 80), dying in 17 days, had not developed esophagitis. Weight loss and debility were rapid in this group of dogs.

Series III (Table III). Of the 7 dogs with esophagogastrostomy and vagotomy with pyloromyotomy, 6 developed esophagitis above the anastomosis. One dog (No. 38) which did not develop esophagitis in 63 days showed low gastric acidity on histamine stimulation preoperatively and postoperatively (0.0 and 28.0 degrees respectively). A jejunal ulcer was demonstrated in the 1 dog (No. 65) in which a gastrojejunostomy had been done instead of the pyloromyotomy. The distal esophageal stump above the sphincter was normal in every instance (fig. 7).

Series IV (Table IV). Nine of the 10 dogs which were reoperated upon had developed esophagitis above the original anastomosis by the time of the reoperation. When the proximal esophagus was moved back over the sphincter by reanastomosis to the distal esophageal stump the esophagitis in 8 of the 9

FIG. 8. Photograph of specimen of stomach and esophagus of dog no. 82 (Series IV). The esophagus, which had been affected with esophagitis, has been reanastomosed to the distal esophageal stump above the sphincter and has become normal as seen in the left upper portion of this photograph. The esophagogastric pouch (lower right) still shows esophagitis with ulceration.

dogs disappeared and healed (fig. 8). One dog died early after reoperation. The remaining esophagus at the esophagogastric pouch remained diseased or became increasingly ulcerated, and perforated in one instance.

In every instance in all series of experiments the esophagus above the sphincter or esophagocardiac junction remained normal without any evidence of esophagitis.

DISCUSSION

Several interesting observations can be made from the results of this study. First, it is evident that the normal and intact esophagogastric junction of the dog is important in protecting the esophagus above it and preventing reflux esophagitis. In almost every instance when the junction is by-passed by anastomosis, the unprotected esophagus develops esophagitis, erosion, and, occasionally, ulceration with perforation. The severity of the involvement seems to be somewhat related to the degree of gastric acidity, in that the least involvement occurred in those animals with the lowest acidity following histamine stimulation.

Second, it is clear from these studies that vagotomy with or without pyloromyotomy does not prevent the development of esophagitis above the esophagogastric anastomosis. Actually, the animals in Series II (esophagogastrostomy with vagotomy) lost weight and became debilitated more rapidly than did those in either Series I or Series III. Moreover, the debility was so great that only 1 dog in Series II could be used for reoperation and re-establishment of continuity. The Hollander (insulin) test for gastric acidity indicated a complete vagotomy in all animals tested.

The esophageal erosions and ulcers, as well as the jejunal ulceration in the 1 dog with gastrojejunostomy, indicate the susceptibility of those respective mucosal linings to gastric secretions when abnormal communications are created. This is significant when it is considered that the dog is an animal in which spontaneous ulceration does not occur. It is likely that prolonged gastric acid hypersecretion with chronic histamine stimulation would intensify all the findings observed in these experiments.

The continence of the esophagogastric junction, demonstrated in these animals, probably is accountable to a physiologic sphincter, independent of the diaphragm. Studies pertaining to the nature of this sphincter are in progress.[7]

If one assumes that the esophagogastric sphincter of the human is similar to that in the dog, the remarkable continence which protects the esophagus from erosion and esophagitis should be preserved whenever possible, in the surgery of the esophagus. For patients with cardiospasm the complication of esophagitis following surgical ablation of the esophagogastric junction does not seem equitable. On the other hand, if it can be shown conclusively that a jejunal segment surgically interposed between esophagus and stomach in patients with severe cardiospasm will act as a functioning sphincter to protect the sensitive esophageal mucosa, then such intervention probably is justifiable. The present aim for surgery of cardiospasm, until the exact physiologic defect is understood and

correctable, should not be mutilation of an already malfunctioning sphincter, but substitution of a similar type of sphincter.

SUMMARY

A brief resumé of the historic and clinical features of cardiospasm is presented. Since surgical procedures for cardiospasm deliberately incise, revise, excise, or by-pass the esophagogastric junction and result in a high incidence of esophagitis, a study of the competence of this sphincter is reported.

The esophagogastric sphincter in dogs protects the esophagus from the development of esophagitis which regularly occurs after esophagogastrostomy. Vagotomy with or without pyloromyotomy does not prevent esophagitis above an esophagogastrostomy in dogs.

Certain criteria for surgical operations for cardiospasm are suggested.

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ACUTE PERFORATED PEPTIC ULCER: AN ANALYSIS OF EIGHTY-SEVEN CASES*

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This study represents an analysis of the patients with perforated peptic ulcer who were admitted to the University of Arkansas Hospital, a charity institution, from Jan. 1, 1947, until Jan. 1, 1955. In order to secure an over-all picture, patients who were admitted moribund as well as discovered at autopsy, are included. A total of 87 perforations occurring in 84 patients were available for consideration.

Perforations occurred 80 times in males and 7 times in females, a respective incidence of 92 and 8 per cent. There were 59 white and 25 Negro patients, a ratio of 2.3 to 1, which is about the relative proportion for total hospital admissions on the surgical service. A slight increase was shown for the spring and fall months, 61 per cent occurring during these periods.

While acute perforation of a peptic ulcer may occur at any age, it is primarily a complication of midadult life. Our youngest patient was 17 and the oldest 78 years of age. The mortality rate increases with advancing years, being especially high after 60 years of age. No deaths were encountered under the fifth decade of life. Age incidence and mortality rates are graphically illustrated in figure I.

The mortality is closely related to the number of hours elapsing from onset until admission to the hospital. No deaths were encountered in 37 patients who were admitted within 6 hours of their perforation. One death occurred in 18 patients who were admitted 6 to 12 hours after perforation. Three deaths occurred in 16 patients who were admitted 12 to 24 hours following perforation. There were no deaths in 4 patients who were admitted 24 to 48 hours after perforation. Of 7 patients who were admitted over 48 hours after onset, 1 died. Perforations occurred in 5 patients during hospitalization. Two of the latter succumbed, 1 being unrecognized for 36 hours and the other being discovered only at autopsy. As has been observed previously by others, it is surprisingly dangerous for one to perforate his ulcer while in the hospital. Ulcer patients carefully examined on admission may afterwards receive medication for recurring pain without adequate inspection. Similarly, patients who were admitted for other reasons may remain unrecognized.

PAST HISTORY

A past history suggesting peptic ulcer was given by 66 (78 per cent) of the patients. Symptoms had been manifest for less than 1 year in 8 patients, from

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1 to 5 years in 32 patients and over 5 years in 27 patients. Few had been under a supervised medical regimen. Previous perforations had occurred in 8 patients (9 per cent). Forty-one patients, or 48 per cent, were experiencing an exacerbation of symptoms at the time of perforation. These symptoms often were severe for the few preceding days. In 19 patients (22 per cent) the first symptoms of peptic ulcer were noted with the acute perforation.

SYMPTOMS

Abdominal pain was the initial symptom in every patient. Onset usually was sudden and severe. It occurred during an alcoholic debauch in 8 patients. While the initial pain usually is epigastric (51 per cent) it is not necessarily so. The initial maximal pain involved primarily the right abdomen in 19 per cent, was generalized in 18 per cent, involved primarily the lower half of the abdomen in 7 per cent, and in 5 per cent involved primarily the left abdomen. Pain was referred into one or both shoulders in 22 per cent. Nausea and vomiting was an early manifestation in a majority of patients, occurring in 58 patients or 69 per cent. Gastrointestinal bleeding manifested as hematemesis or melena was an accompanying symptom in 6 patients or 7 per cent. It was considered as a serious complication in only 1 patient.

PHYSICAL EXAMINATION

Abdominal rigidity was the most consistent positive finding, being present in 76 patients and absent in 11. Peristalsis was recorded as present in 39 and absent in 28. Shock rarely is seen early in the course of this complication. There were only 3 patients with perforation under 24 hours in whom shock was present. Its presence usually indicates an ominous prognosis. The leukocyte counts varied from 3,750 to 35,000 per cu. mm. While there usually is an elevation in the leukocyte count with a shift to the left in the differential within 6 hours

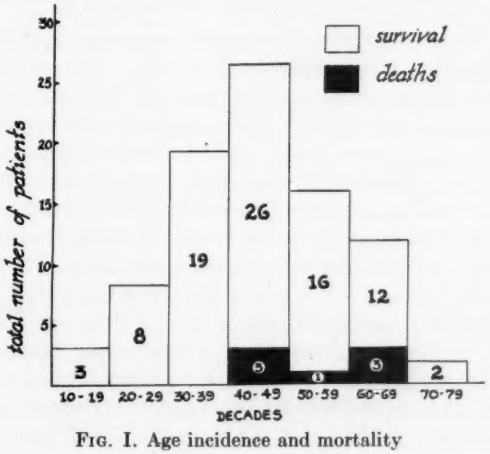

FIG. I. Age incidence and mortality

after perforation, these findings are nonspecific and add very little in establishing the diagnosis. A low count in a late perforation usually offers a bad prognosis. Red blood count and hemoglobin determinations were of little significance except in hemorrhage or as a reflection of hemoconcentration in dehydration.

ROENTGENOLOGIC FINDINGS

A very helpful aid in diagnosis is the determination of the presence or absence of free air in the peritoneal cavity. An upright or a right lateral decubitus technic may be utilized. Such studies were made in 84 of the 87 cases. Free air was present in 63 patients or 74 per cent. The quantity of free air often is proportional to the duration of symptoms. It may be absent, or present only in small quantities, in early perforations. For this reason, it is important to have the patient maintain the upright or the right lateral decubitus position for a number of minutes before taking the roentgenogram. Such studies also may be useful in management. On two occasions, patients were admitted over 24 hours after onset of symptoms in whom it was suspected that the perforation had spontaneously sealed. Nonoperative therapy was instituted. In one no air was present initially but appeared a few hours later and in the other the initial quantity of air increased. At operation, both were found to have leaking perforations.

SITE OF PERFORATION

The duodenum was the site of perforation in 67 instances and the stomach in 15, a ratio of slightly over 4 to 1. The location was undetermined in 5 patients. The duodenal perforations were all in the first portion on the anterior or superior surfaces. Of the gastric lesions, 13 were immediately prepyloric and 2 were located near the midportion of the lesser curvature on the anterior surface. While the diameter of the perforations varied from 2 mm. to 2 cm., the vast majority were 3 to 5 mm. in diameter.

ANALYSIS OF SURGICALLY TREATED PATIENTS

Seventy-three patients (84 per cent) received operative treatment. The general policy during the period of this study was to consider the perforation of a peptic ulcer as a surgical emergency requiring closure. A Levine tube is immediately placed in the stomach and constant suction applied while roentgenograms and other diagnostic measures are under way. Parenteral fluids are given when indicated to combat dehydration, electrolyte imbalances or shock. Penicillin and streptomycin were administered to most of the patients although sulfadiazine rather than streptomycin was given to a few patients earlier in the series. Unless the patient's general condition required a longer period for preoperative preparation, an interval of 2 to 4 hours elapsed until operation. The significance of this initial essentially nonoperative treatment will be referred to later. Routinely at present, under general anesthesia, a short upper right rectus incision is employed and the perforation is closed with an omental graft after the method of Graham.[7] Omentum carried with its blood supply is preferred to a free graft.[16] In a few instances early in the series, suture methods with and without omental

TABLE I

Relation of mortality rate to the time of operation

Hours from Onset of Perforation to Operation	Total Number of Cases	Number of Deaths
0–12	39	1
12–24	23	2
Over 24	11	2
Total	73	5

reinforcement were employed. A subtotal gastric resection was done on 3 patients as primary treatment. Two had been hospitalized for exacerbation of long standing ulcer symptoms at the time of perforation. One of these had associated obstruction. The third patient had concomitant bleeding and obstruction. These 3 patients survived and remain free of symptoms.

The duration from onset of symptoms until operation and increasing mortality rate in delayed treatment are depicted in table I. The preoperative diagnosis was correct in 67 cases and incorrect in 6. Incorrect preoperative diagnoses were acute appendicitis in 5 instances and generalized peritonitis of undetermined etiology in 1 instance. During the period of this study, there were 4 diagnoses of perforated peptic ulcer preoperatively which were in error. The correct diagnoses were acute cholecystitis in 2 cases, acute pancreatitis, and acute pneumonitis.

While the operator's gross impression as to the effectiveness of spontaneous sealing of a perforation may sometimes be in error even with special technics[18] an analysis of this feature deserves some merit. This was of particular interest as the majority of patients had received nonoperative treatment measures (constant suction) from admission until operative intervention. A period of 2 to 4 hours usually was required although as long as 24 hours intervened in certain instances. The perforation was found to have sealed spontaneously in 11 instances and to have remained unsealed in 47. No comment was made by the operator concerning this status in 14 cases. Of the 13 patients with gastric lesions, spontaneous sealing had occurred in only 2 instances with respective durations of perforations of 13 and 26 hours. The remaining 11 gastric perforations were found unsealed even though periods over 24 hours had elapsed in some instances since perforation (table II). This notorious tendency for gastric

TABLE II

Status of gastric perforations at operation

Onset to Operation (Hours)	Sealed	Unsealed	Total
0–6	0	3	3
6–12	0	1	1
12–24	1	4	5
Over 24	1	3	4

TABLE III

Status of duodenal perforations at operation

Onset to Operation (Hours)	Sealed	Unsealed	Total
0–6	0	8	8
6–12	2	13	15
12–24	3	12	15
Over 24	4	4	8

perforations to remain open has been noted by others to constitute one of the major hazards of nonoperative therapy.[8] The status of duodenal lesions in this regard is shown in table III. No perforations were found sealed within 6 hours and only 5 of 38 perforations under 24 hours were effectively sealed at the time of operation. Of those of over 24 hours duration, 4 were sealed and 4 unsealed.

Serious complications developed in 6 patients in the operative series, an incidence of 8 per cent. Complications were multiple in several. Peritonitis developed in 3, subphrenic abscess in 2, a wound infection in 2, a wound dehiscence in 1, a pelvic abscess in 2, and reperforation 5 days following closure in 1. The most common nonserious complication was an area of patchy basilar atelectasis or pneumonitis which subsided spontaneously within a few days.

ANALYSIS OF NONOPERATIVE TREATED PATIENTS

A total of 14 patients were treated nonoperatively. Nine patients with symptoms over 24 hours presented a clinical picture indicating sealed perforations. One patient refused operation. Nonoperative therapy was elected in 1 elderly woman whose ulcer perforated in the hospital and was recognized within 2 hours. This method was chosen because the patient was in cardiac decompensation complicated by bilateral bronchopneumonia. Free peritoneal air was demonstrated in 75 per cent. All were subsequently proved to have duodenal ulcers on roentgenologic examination. Seven have since been subjected to elective subtotal gastric resection. No complications nor deaths occurred in this group of patients.

In 2 patients, nonoperative therapy was instituted believing spontaneous sealing of the perforation had occurred. The clinical course and roentgenologic studies indicated however that this assumption was incorrect. At operation, the presence of leaking perforations was verified. Both patients made an uneventful recovery.

One patient entered the hospital in a moribund state 72 hours after perforation and died within 8 hours.

An unsuspected duodenal perforation was found at autopsy in another patient who had associated cirrhosis of the liver with primary hepatic carcinoma which had metastasized to the lungs.

ANALYSIS OF MORTALITY

Including the unsuspected case discovered at autopsy and the patient admitted in extremis, there were 7 deaths occurring in the 87 perforations giving

TABLE IV

Analysis of deaths

Age	Sex	Time to Operation	Location and Ulcer Status at Operation	Cause of Death
66	M	27 hrs	Gastric, not sealed	Death 12th postoperative day; Peritonitis, wound infection & dehiscence, ? pulmonary embolus, no autopsy
63	M	36 hrs	Duodenal, not sealed	Death 18 hrs. postoperative. Shock, peritonitis, reperforation 5 days after initial closure and uneventful course. Unrecognized 36 hours
64	M	19 hrs	Gastric, not sealed castor oil in free peritoneal cavity	Death 11 hrs. postoperative. Shock and peritonitis
56	F	48 hrs	Gastric, not sealed castor oil in free peritoneal cavity	Death 6 hrs. postoperative. Shock & peritonitis. Entered hospital in shock 24 hrs. after onset. Resuscitation measures 24 hrs. Marked obesity
40	F	12 hrs	Duodenal, not sealed	Anesthetic death in operating room. Anoxia.
40	M	No operation	Duodenal, unsealed. Autopsy	Peritonitis. Death 8 hrs. after admission. Entered hospital in extremis 72 hrs. after onset
46	M	No operation	Duodenal, unsealed	Discovered only at autopsy. Generalized peritonitis. Cirrhosis and primary carcinoma of liver metastatic to lungs

an over-all mortality rate of 8 per cent. These are considered individually in table IV. In the 73 patients who were operated upon, there were 5 deaths, a mortality rate of 6.8 per cent. Three of these deaths represent errors of judgment in the patients' ability to withstand an operative procedure at the selected moment as death from shock and peritonitis ensued within a very few hours postoperatively. It is interesting to note that 2 of these patients had taken castor oil just prior to hospitalization and at operation were found to have a fulminating peritonitis with oil floating in the free peritoneal cavity. This may have influenced their fatal termination. One death is attributed to an anesthetic accident. Two deaths occurred in the nonoperative group, 1 in a patient admitted moribund and 1 discovered only at autopsy. In reality these received no treatment. If these latter 2 deaths are excluded, there was a mortality rate in the treated patients of 5.9 per cent.

FOLLOW-UP

Of the total of 84 patients, 7 succumbed and 3 were subjected to primary gastric resection. Twenty of the remaining 74 failed to keep return clinic appointments and cannot be traced. Twenty-four have been followed for under 1 year. Sixteen remained symptom free on medical therapy. Eight had persistent symptoms. Definitive operations were done in 6 of the latter within the year. One was subjected to vagotomy elsewhere, and 5 were subjected to subtotal gastric

resection at this hospital. Thirty patients have been followed from 1 to 7 years. Ten have been virtually symptom free on medical therapy. Twenty have developed symptoms of varying degrees of severity. Seven of the latter have now had subtotal gastric resections. Of a total of 54 patients of whom we have some knowledge of their subsequent course after perforation 13 (24 per cent) have already required a definitive operation. This number will certainly increase with the passage of time.

DISCUSSION

A number of studies have reported in recent years a reduced mortality and morbidity in the management of acute perforated peptic ulcer by simple closure.[2, 4, 12, 13] There also have appeared reports indicating that nonoperative management is quite successful.[8, 20, 22] In European clinics for many years and in this country more recently, it has been shown that subtotal gastric resection may be done with a low mortality role for an acute ulcer perforation in selected cases.[1, 3, 6, 10, 21] Improved supportive measures, including parenteral fluids and electrolytes, whole blood, gastric suction, and antibiotics, have all contributed to this improved status.

Long term follow-up reports [9, 23, 24] have demonstrated that, contrary to earlier belief, most of these patients eventually develop further symptoms. A number may succumb from complications which might have been prevented by definitive surgery. In Turner's series, 38.5 per cent required additional surgery. In our small series, 24 per cent have already required definitive surgery. Definitive surgical measures can be expected to give quite satisfactory results in 80 to 90 per cent of patients.[5, 14, 15, 17, 19]

There have arisen from these studies advocates of nonoperative vs. operative management, primary subtotal gastric resection vs. simple closure, and delayed resection after simple closure or nonoperative management. Our experiences lead us to believe that no one routine is correct in all instances but that a selection of patients for the various alternatives may prove the more nearly perfect answer to the problem. A number of our patients could have been saved the time and jeopardization of a second operation plus an immeasurable degree of anxiety and discomfort if a primary resection had been done at the time of perforation. On the other hand, a number were subjected to an operation, simple closure, which accomplished nothing more than nature had already completed. A definitive operation, if indicated in this latter group, could most prudently be done after recovery from the acute episode. The results of definitive surgical measures do not seem excellent enough, however, to advocate their use in every patient having a perforation, especially when 25 per cent[11] may remain symptom free.

The conclusion reached from this study is that the vast majority of acute perforations should continue to be managed by simple operative closure. Immediate results are excellent. Most patients are treated within the first 24 hours when the perforation has not sealed spontaneously. Differentiation between gastric and duodenal perforations is impossible. A definitive diagnosis is made early. Very few of our patients have previously been on a satisfactory medical

regime. Indications for primary subtotal gastric resection should be cautiously extended at this institution. Patients with an early perforation who are in good general health should be considered for this procedure if there is a long ulcer history with a reasonable trial of medical therapy or a previous severe complication. A gastric perforation also should be given this consideration. A resection is almost mandatory if there is concomitant serious bleeding or obstruction.

We are reluctant to advocate a nonoperative plan of management in any patient with symptoms under 24 hours duration because of the desirability of an early accurate diagnosis and the high incidence of unsealed ulcers demonstrated in this series. After this period of time has elapsed, some selection of cases may be properly made, nonoperative treatment being instituted in patients in whom it is thought that recovery is occurring. Very close observation must be maintained to assure that this assumption is correct. Occasionally other complicating diseases will dictate nonoperative therapy in early perforations if the patient appears unable to withstand an operative procedure. If the patient's general condition is precarious as a result of the perforation, nonoperative therapy is preferred. In retrospect, is believed that 3 of the deaths in the group of patients who were operated upon of this series might have been prevented had nonoperative measures been continued. At least it seems this would have been their only chance for survival.

While this series of 87 perforations with an over-all mortality rate of 8 per cent and a mortality rate of 5.9 per cent in treated patients is too small to accurately determine mortality rates, it does seem to agree with the trend in other reports showing improvement has occurred in recent years. In a similar unreported study of 58 consecutive perforations seen at this hospital from 1940 to 1947, the over-all mortality rate was 34 per cent and the mortality rate in the operative group was 22 per cent. On the other hand, in the last 6 years of the current study in 66 consecutive cases, there has been an over-all mortality rate of 3 per cent all in the group of patients who were operated upon.

Results of treatment in case studies made prior to the last 10 years should not be used as a comparison for variations in methods of modern day treatment.

SUMMARY

An analysis of 87 consecutive acute gastro-duodenal peptic ulcer perforations seen at the University of Arkansas Hospital, a charity institution, is presented. Routine statistical studies are in agreement with other recently reported similar series.

The over-all mortality rate including patients who were admitted moribund and those discovered at autopsy was 8 per cent. In treated patients, the mortality rate was 5.9 per cent. In the last six years of the study in 66 consecutive cases, the over-all mortality rate has been 3 per cent.

Operative treatment is advocated in patients with symptoms under 24 hours duration. Simple closure of the perforation is the procedure of choice in the majority of patients. In selected cases, a primary definitive procedure (subtotal gastric resection) is indicated.

Nonoperative management is the treatment of choice in selected cases after 24 hours has elapsed from onset of symptoms.

Results of treatment of perforated peptic ulcer have markedly improved at this institution during recent years. In a similar study of the previous 7 year period, there was an over-all mortality rate of 34 per cent.

While follow-up studies are incomplete, it is known that subsequent definitive surgery has already been required in 24 per cent of the patients in whom follow-up information is available.

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SOLITARY POLYPS OF THE COLON AND RECTUM: A STUDY OF INHERITED TENDENCY

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INTRODUCTION

It has become increasingly evident from the recent literature that adenomatous polyps of the colon and rectum are premalignant lesions and, as suggested by Lahey,[4] that they are the precursors of most, if not all, carcinomas of the large bowel. It is also a well established clinical fact that there are certain families which exhibit an abnormally high incidence of organ-specific cancer, such as carcinoma of the colon[3, 7] or breast.[8]

If these two factors are correlated, it leads to the interesting hypothesis that a family with an abnormally high incidence of cancer of the large bowel should also exhibit an abnormally high incidence of benign adenomatous polyps. This correlation is known to be true for families with familial or "*multiple*" polyposis but to our knowledge the hypothesis has never been investigated in instances of solitary adenomatous polyps.

Utah, because of its unusual religious background, which sanctioned polygamous marriage for some 50 years, provides unique families of great size on which to investigate such a hypothesis.

Since 1950 the Laboratory of Human Genetics, University of Utah, has been actively studying genetic patterns in human cancer. One family, kindred 133, was initially reported[3] to have had 33 per cent (6 of 18) adult offspring die from gastrointestinal cancer. Four of these tumors definitely originated in the large bowel. Because of this unusually high frequency of carcinoma, this family was selected for investigation of the possible correlation between the incidence of carcinoma and the incidence of adenomatous polyps of the colon and rectum. An initial report of the genetic aspects of the study was made in 1955[9] and the following is a summary of clinical data obtained to date.

MATERIALS AND METHODS

Kindred 133 is illustrated in figure 1. It's original male progenitor, I-1 had four wives. He apparently died of a malignant melanoma of the leg but none of the wives was suspected of having malignancy. Of his 24 children, 18 lived to adult life and 6 of these (II-2, 4, 6, 13, 20, 21) died of carcinoma of the gastrointestinal tract. Four of the carcinomas were reported as cancers of the rectum or colon and two were reported as abdominal carcinomatosis thought to be primary in the stomach. However, postmortem examination was not done on

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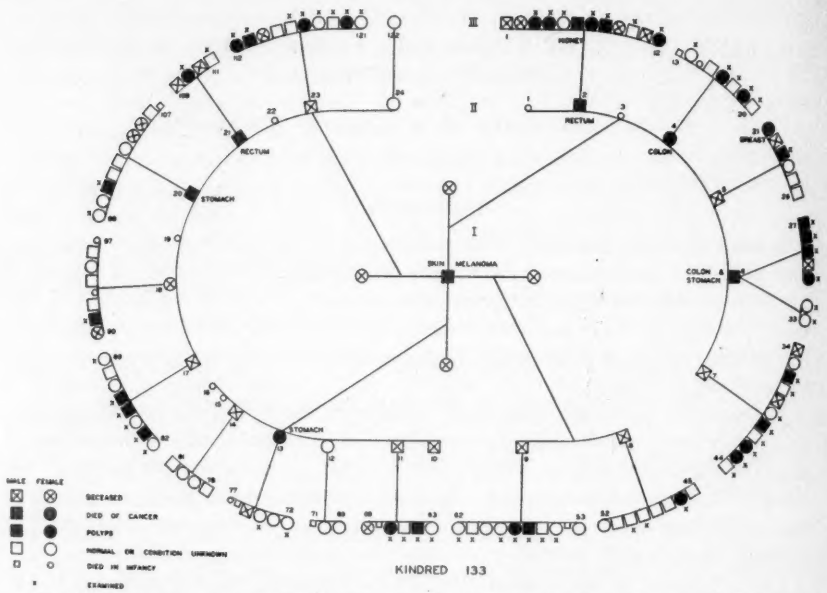

FIG. I. Pedigree chart of Kindred 133 showing the distribution of polypoid lesions of the colon and rectum and of deaths due to cancer.

either of the later patients. The 18 children produced 122 third generation children. One of this group has died from carcinoma of the kidney, 1 from carcinoma of the breast, and 2 are known to have had large bowel polyps. At present, 96 of these individuals are living and approximately two-thirds reside in the State of Utah. They range from 24 to 72 years of age with an average of approximately 52 years. There are in addition 152 fourth generation children over the age of 20 now available for study.

The study was planned to provide a general history and physical examination for each interested individual. Sigmoidoscopy, hematocrit, and stool guaiac also were included. Barium enema with air contrast studies has been offered to all patients found to be positive for polyps on sigmoidoscopy. Re-examination at a 12 to 18 month interval is now being carried out on the initial group of third generation patients. Examinations also have been initiated on available fourth generation children over 20 years of age. In addition, interested spouses of third generation patients have been given similar examinations as a control group to study environmental factors.

RESULTS

Third Generation: Results in third generation children are summarized in table I. Sixty-two of the 96 living third generation children have been examined. Thirty-one of these patients (50 per cent) have been found to have one or more adenomatous polyps in the distal 25 cm. of colon and rectum. The ages of posi-

TABLE I

Results in third generation

Number third generation patients examined	62
Number third generation patients with polyps	31
Per cent of patients with polyps	50%
Number positive patients re-examined	20
Number positive patients with new polyps	14
Per cent of patients with new lesions	70%

tive patients range from 26 to 70 years with an average of 52 years. The average age of the negative group was 52 years. Twenty-nine males and 33 females were examined with 16 males and 15 females found to be positive for polyps. Nine patients had from 2 to 4 polyps on sigmoidoscopy. Twenty-two, or 71 per cent, had only solitary lesions.

Thus far, 14 of the 18 secondary family groups have been sampled. Child II-10 had no children and the families of II-12, II-14 and II-24 have not been examined. Of the 14 family groups studied, 13 have had 1 to 4 members of the third generation positive for polyps. The heaviest concentration, however, is in the family of II-6 who himself died of colon carcinoma. All 4 of this man's children by his first wife were positive while the 2 by his second wife were negative. The 3 positive males in this group also were the only patients with more than 2 polyps. Each had 3 or 4 lesions and in the 2 re-examined, both had multiple new polyps at the end of 18 months.

Re-examination after a 12 to 18 month interval has been carried out on 30 third generation patients thus far. Twenty of these patients were positive on first examination and 14, or 70 per cent, have been found to have new lesions on re-examination. Three of the 10 patients who were negative on first examination were found to have lesions when restudied.

Fourth Generation: Results in fourth generation children are summarized in table II. Examination of the fourth generation children over 20 years of age

TABLE II

Results in fourth generation children and third generation spouses

Number fourth generation patients examined	12
Number fourth generation patients with polyps	2
Per cent fourth generation patients with polyps	16.7%
Number of spouses examined	22
Number of spouses with polyps	1
Per cent of spouses with polyps	4.5%

has recently been initiated and to date 12 members have been examined. Two patients, 27 and 30 year old females, have been found to be positive. These patients are the daughters of III-12 and III-27, both of whom have shown polyps on both first and second examinations. Also both of their grandparents, II-2 and II-6, died of carcinoma of the large bowel.

Character of the Polyps: All polypoid lesions were removed for pathologic examination. Of the 64 polyps removed from these patients, all but 2 have been small, measuring 2 to 7 mm. in diameter. One lesion removed prior to the study was 1.5 cm. in diameter. Twelve were pedunculated and the remaining 52 were sessile. None was palpable on digital examination. Their level in the rectum above the anus was 10 to 24 cm. with a mean of 16 cm. None obtained during the study appeared grossly malignant and in none was there history or physical findings to suggest inflammatory origin.

A simple pathologic classification of polyp, hyperplastic polyp, carcinoma in situ, and invasive carcinoma has been used. No invasive carcinoma has been found. Two polyps showing carcinoma in situ were removed from patients III-17 and III-19 prior to the beginning of this study. Ten lesions were classified as showing hyperplastic change and the remainder as simple polyps. Three small lesions, although grossly polypoid, were reported as normal by the pathologist.

A very interesting type of hyperplastic "*tufting*" has been found in the surface and gland mouth epithelium of 16 of the 31 positive patients. This is illustrated in figure 2. The change is characterized by elongation of cells with some piling up of nuclei to produce papillary fronds of epithelial cells. There is little or no demonstrable stroma or vascularity in the stalks of these projections and the involved nuclei appear essentially normal. The change apparently begins in the surface epithelium or near the gland orifice and then extends gradually into the deeper portions of the mucosa. It appears to represent the initial form of polyp development in this group and it is under more intensive study at the present time.

FIG. II. Photomicrograph showing the papillary "*tufting*" found in the rectal surface mucosa of many members of Kindred 133.

History, Physical and Laboratory Findings: Histories have been essentially noncontributory. Only 1 patient with a sigmoid polyp removed prior to the study gave a history of symptoms suggestive of colon disease. Ten patients gave a history of some type of rectal bleeding. None of the bleeding was of recent origin and 5 of the group were negative for polyps. Seven patients had an established history of peptic ulcer, and 11 had histories of hemorrhoids. Only 2 were found to have significant hemorrhoids on examination. Six members have some type of detectable benign neoplasm of the skin or subcutaneous tissue at present, and one has a carcinoma of the skin.

Most of the family were raised in an endemic goiter area in southeastern Utah and 30, or 48 per cent, have palpable nodular thyroids.

Barium enema with air contrast study has been done on 17 of the 31 patients positive for polyps on sigmoidoscopy. One patient has been found to have 2 additional sigmoid polyps which he has thus far failed to have removed.

Hematocrit and stool examinations have been of no value in predicting the presence or absence of polyps.

Spouse Study: The results of the spouse study are summarized in table II. As a control on environmental factors, the spouses of 22 third generation children have been examined. They have lived with their present mates in a similar environment from 9 to 41 years with a mean of 23 years. Only 1 had a polypoid projection on sigmoidoscopy and this was reported as normal mucosa by the pathologist.

DISCUSSION

Several factors strongly suggest that the increased incidence of polyps in this family group is due to a definite familial trait and not merely due to a chance finding. First, there is a history of a 33 per cent incidence of carcinoma of the gastrointestinal tract in the second generation children. Second, the 50 per cent incidence of adenomatous polyps in the third generation children is extremely high and is 5 to 10 times greater than that reported in the literature for groups of asymptomatic patients of similar age. Third, there is a suggestion that this trait will be carried into the fourth generation since 2 of the 12 children (16.7 per cent) already have been found to have polyps. The disease involves 13 of the 14 sibships studied in the family and involvement with cancer or polyps can be demonstrated in 3 generations in at least 2 cases. This suggests that a form of dominant inheritance is involved. The 50 per cent incidence in the third generation further suggests that the male progenitor (I-1) of the kindred was homozygous for this dominant gene. However, this hypothesis can only be tested by getting more data on subsequent generations.

It also appears that the family is afflicted with solitary or occasional polyps and not with the known hereditary disease of familial polyposis. Cancer deaths in the second generation children occurred at the average age of 63, which is consistent with the age of cancer deaths in the general population and not with the age of 41.6 years reported for patients with familial polyposis.[5] Also, the age distribution, sex distribution and number of patients with solitary or multiple lesions are similar to that reported for patients with solitary adenomatous

polyps. The relative infrequency of lesions above the rectosigmoid and the rather complete absence of symptoms also are characteristic of the solitary polyp and not familial polyposis.

This family represents, to our knowledge, the first reported instance in which solitary or occasional discrete polyps of the colon and rectum have shown a hereditary tendency. The data presented strongly support the original hypothesis of this study correlating a high incidence of benign polypi with the established family history of a markedly increased frequency of large bowel carcinoma. The high incidence of polyps provides an adequate answer as to why carcinoma of the large bowel was so frequent in the second generation children. It also provides one additional bit of evidence to support the already well-established idea that benign polyps are the precursors of most, if not all, large bowel carcinomas.

The high frequency of new polyps appearing in 14 of 20 positive patients re-examined after 12 to 18 months is another indication of the extremely active polyp formation in this group. It is 2 to 4 times greater than the 12 to 45 per cent incidence reported in the literature[2, 5, 6] for development of new polyps in patients with previously diagnosed solitary lesions. It is possible that occasional small polyps may be missed on the initial examinations, but the majority of the new lesions were in obvious areas and not hidden behind valves or in mucosal folds. In no instance was there evidence of recurrence of polyps in the areas from which lesions were previously removed for biopsy with cautery of the base. The extreme rate of recurrence would appear to have its practical implications only for the family reported, and would suggest the necessity for more frequent examination than usually is recommended for the patients with solitary polypoid disease.

The significance of the papillary tufting illustrated in figure 2 is unknown. It is interesting that areas showing this phenomenon can frequently be detected grossly by a slight paling of the mucosa and that the stages from normal mucosa through tufting to full sessile polyp can be predicted grossly. This progression of events suggests that the tufting effects may be the initial stage of polyp formation and the basic pathologic defect in this family group.

Roentgenologic examinations still are incomplete with only 17 patients being examined thus far. The finding of polyps in only 1 patient or, 6.2 per cent, by barium enema and air contrast study appears abnormally low. However, this might be partially expected because of the small size of the lesions encountered on sigmoidoscopy.

The concomitant study of spouses of this family group has been of interest as a control on environmental factors. Twenty-two spouses living in a similar environment for an average of 23 years provide suggestive evidence that environmental factors, such as diet and water, play little or no part in the initial etiology of the adenomatous polyp. However, the place of environmental factors in production of malignant degeneration in the benign adenomatous polyp still may be questioned. The one measurable environmental effect in the two groups is that of nodular goiter and the family members show an incidence of 48 per cent while their spouses show only 40 per cent. The difference apparently arises

from the fact that a few of the spouses were raised through early life in areas outside the endemic goiter area in which members of the original family are concentrated.

The importance of the above study to the family group under consideration is obvious. Theoretically, by removal of all polyps in the benign stage, carcinoma of the large bowel could be virtually eliminated from the family. Practically this is impossible. However, with two-thirds of the third generation under careful follow-up study by sigmoidoscopy and roentgenogram, the unstudied one-third of the family should provide an interesting comparison group to help determine the effectiveness of our established methods of treatment and control of solitary polyps.

Certainly, on the basis of a single family study, it cannot be postulated that all solitary adenomatous polyps have a hereditary background. On the other hand, we have found no evidence in the literature that adequate clinical studies have been made to disprove this possibility. Human families are so small and often so scattered that such studies would be relatively useless or impossible in most areas of the world. Because of the availability of large family groups in the Utah area and the excellent geneological records, further studies of families with a high incidence of rectal carcinoma are in progress. It is hoped that either supporting or conflicting evidence may be provided to clarify the position of heredity in the etiology of the solitary lesions. Prolonged follow-up of this group and its subsequent generations also may help to establish some definite genetic pattern.

The clinical implication of such a possibility as a familial trait in the origin of solitary polyps is obviously important. In addition to the frequently advocated routine sigmoidoscopy on all hospital and office patients, certainly a more adequate family cancer history should be obtained. It is not infrequent to find that two or more members of a family have succumbed to large bowel carcinoma. In such a family it would seem just as advisable to advocate a family survey of adult members as to continue routine, long term follow-ups on the individual patient with known polypoid disease.

SUMMARY AND CONCLUSIONS

A clinical study of a large family group with an abnormally high incidence of death from large bowel carcinoma is presented. Thirty-three per cent of adult second generation children died from gastrointestinal carcinoma. In attempting to correlate this fact with the presence of adenomatous polyps of the colon and rectum, 62 third generation children were examined by sigmoidoscopy and roentgenogram. Thirty-one, or 50 per cent, were found to have small adenomatous polyps of the rectum or rectosigmoid. The age and sex distribution of the patients and the character of the lesions was similar to that seen in other reported studies of solitary polyps of the large bowel. Two of 12 fourth generation children examined also have been found to have polyps and 14 of 20 third generation patients re-examined after 12 to 18 months were found to have new lesions.

The findings strongly suggest a definite familial trait in the occurrence of

solitary polyps in this group and provide an adequate explanation for the high incidence of large bowel carcinoma in the original family. A form of dominant inheritance is suggested. The implications of a possible familial factor in the etiology of solitary polyps of the large bowel and their applications to clinical cancer detection are discussed.

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THE SURGICAL TREATMENT OF SIGMOID DIVERTICULITIS

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The therapy of diverticulitis of the sigmoid colon has become more aggressive in recent years. In the past, acute diverticulitis was commonly treated by supportive medical measures. If complications developed, they were treated by palliative operations with the hope that diverticulitis or its complications would not recur. These palliative measures usually involved diversion of the fecal stream and late restoration of bowel continuity. Excision of the diseased segment of colon was rarely done.

The importance of sigmoid resection in treatment of the disease was emphasized by Smithwick[7] in 1942. He reported poor late results in patients who had operations other than resections, since 78.9 per cent required further surgery for recurrent disease and 12.5 per cent of them died of their disease. The superior results of sigmoid resection in the treatment of diverticulitis have been confirmed by many others including Pemberton,[5] Boyden,[1] Colcock,[2] Lewis and Hurwitz[3] and Welch and Allen.[9]

Important factors that have led to revision of older methods of therapy include a lower mortality rate in resection of the sigmoid colon and a better understanding of the complications of diverticulitis. In two earlier reports[3, 8] we have urged a more aggressive attitude in the surgical treatment of diverticulitis, since we believe that resection of the involved colon offers greater likelihood of cure with lower mortality and morbidity rates. It is our belief that the indications for resection of the diseased colon should be enlarged.

This report presents our recent experiences with surgical treatment of 23 patients who had sigmoid diverticulitis, 15 of whom were treated by primary resection without colostomy. In the other 8 patients simultaneous colostomy was done twice and preliminary colostomy 6 times. The 6 patients had sigmoid resections from 3 to 12 weeks after the colostomy. Of the 23 patients, 10 were male and 13 were female. The youngest patient was 35 years of age and the oldest 78, the average age being 57. Table I lists the presenting symptoms and complications of diverticular disease, and table II presents the complications following operation. There were two deaths in this series, one resulting from pulmonary embolism and one from a mismatched blood transfusion, giving an operative mortality rate of 9 per cent.

INCIDENCE

The exact frequency of sigmoid diverticulitis in the population at large is impossible to determine. It is usually assumed that diverticula are present in 5 to

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TABLE I

Presenting symptoms and complications in 23 cases of sigmoid diverticulitis

Obstruction	
Partial	12
Complete	4
Perforation	4
Vesical fistula	2
Ileal fistula	2
Rectovaginal fistula	1
Bleeding	
Massive	4
Possible carcinoma	4
Recurrent attacks	4

TABLE II

Operative complications

Evisceration	3
Superficial wound infection	3
Pulmonary embolus	1
Postoperative small bowel obstruction	1
Mismatched transfusion	1

10 per cent of all individuals over 40 years of age and that about one-fifth of these develop clinical diverticulitis. Pemberton, Black, and Maino[6] reported an 8.5 per cent incidence of diverticulosis found in 47,000 barium enemas. In 2000 consecutive barium enemas, Welch and Allen found neither diverticulitis nor diverticulosis in patients below the age of 35. However, from that age upward there was a steady increase in frequency of diverticulosis, and it was noted that the frequency of diverticulitis ascended sharply with age. In the sixth decade, approximately one-fifth of all patients with diverticulosis had diverticulitis, while in the ninth decade, this fraction had increased to one-third. These figures demonstrate that a large feature in the increasing frequency of this disease is the rising average age of our hospital population.

INDICATION FOR OPERATION

The morbidity associated with complications of diverticulitis and the inefficiency of surgical measures other than resection of the diseased colon strongly suggest that sigmoid diverticulitis should be treated by definitive excision. Palliative surgical measures are indicated only to prepare the patient for resection. Indications for surgery in diverticulitis include perforation, obstruction, hemorrhage, recurrent attacks of inflammation, and inability to differentiate diverticulitis from carcinoma.

Perforation furnishes the most common reason for operation. It may present in various ways. There may be walled-off perforations which drain spontaneously into the bowel. These abscesses are frequently associated with exacerbations of diverticulitis and they offer the further hazard of fistula formation between the small intestine and the diseased sigmoid or between the bladder, ureter, and

more rarely the vagina. In the milder forms of perforation with abscess, the symptoms will usually subside under conservative management. The recurrence rate is, however, high. Perforations that involve massive peritoneal soiling make immediate operation mandatory. These are frequently sudden and associated with few premonitory symptoms. We have encountered four perforations with massive peritoneal soiling. All of these patients were treated by immediate operation consisting of complete diversion of the fecal stream, drainage of the peritoneum adjacent to the area of perforation and intensive antibiotic therapy. All recovered and had sigmoid resections and closures of the preliminary colostomies.

Obstruction of the colon is an indication for surgical treatment. The obstruction is most commonly incomplete and results from the pericolic inflammation with fibrosis and narrowing of the sigmoid lumen. Obstruction was present in 16 of our 23 patients. Four patients were completely obstructed and 12 showed partial obstruction. Preliminary diverting colostomy with subsequent resection was used in all patients with complete obstruction and 2 of 12 patients with partial obstruction had colostomies prior to their resections. One of the patients had a simultaneous colostomy. The partially obstructing lesion in 9 patients was treated conservatively by Cantor tube intubation, mechanical cleansing of the bowel and intestinal antibiotics. Primary resection was done in these patients without a death. One patient with complete obstruction had a fatal pulmonary embolism.

Rectal bleeding is not uncommon in diverticulitis; LeRoyer and White[4] reported an incidence of 16.5 per cent in 200 patients. In Welch and Allen's series of 582 patients, rectal bleeding was noted in 27 per cent of the patients who had resection and subsided in all but one instance after the sigmoid had been removed. We encountered massive bleeding in 2 of our 23 patients. Bleeding was controlled by surgical resection in both. In a series of 68 cases, Noer[5] found rectal bleeding in 20. He made injection studies of the excised diverticula and demonstrated within them a striking concentration of blood vessels. The size and distribution of blood vessels within the walls of the diverticula are such as to make severe hemorrhage probable in the event of inflammation or ulceration. His study indicated why massive hemorrhage may complicate diverticulitis. While bleeding is usually infrequent, its magnitude may furnish the major indication for operation. Because it is difficult to rule out coexisting cancer or polyps as a source of bleeding, we favor aggressive treatment of any sigmoid lesion associated with bleeding.

DISCUSSION

There is little difference of opinion that the aforementioned complications of diverticulitis are valid indications for early resection. In addition, we believe that selected cases of alleged uncomplicated diverticulitis are candidates for sigmoid resection. We agree that there is a substantial number of patients who have mild attacks of sigmoid diverticulitis, respond readily to symptomatic treatment and reveal no significant roentgenographic changes in the sigmoid. This group can be treated by conservative measures. However, it is our belief that the patient who has a severe attack of acute diverticulitis, characterized by

elevation of temperature, leukocytosis, tenderness, spasm and positive roentgenographic findings has severe inflammation in the pericolic tissue and the colon wall with permanent, irreversible damage. The extent of this damage represents the degree of vulnerability to repeated attacks of diverticulitis and associated complications. Recurrent attacks of diverticulitis are a real hazard to the life and health of the patient. The longer symptoms persist, the more frequently serious complications will be seen. One is impressed by the pathologic findings at operation in these patients; consistently, they are much more severe than the symptoms suggest. The severity of the chronic inflammatory changes show the irreversibility of the disease process. The findings at operation suggest that acute inflammation in diverticulitis subsides rapidly under treatment with antibiotics and low residue diet, but that the colon is irreversibly damaged by the pericolic and peridiverticular inflammation which produces chronic inflammatory changes out of proportion to the symptomatology. These patients are best treated by a one stage wide resection of the involved sigmoid during a quiescent phase of the disease.

Diverticulitis in a patient under the age of 50 appears in a small percentage of cases. The severity of the disease process warrants early surgical excision. Welch and Allen pointed out that in their series only 6 per cent of all observed cases of diverticulitis occurred in patients under 50 years of age. Of the patients in their series having resection, 18 per cent were under 50 years of age. They further emphasized that the patients who develop urinary symptoms due to diverticulitis are candidates for early resection, particularly the male patients. Urinary symptoms are frequently the premonitory warning of a sigmodovesical fistula. We agree with this observation and believe that, in addition to urinary symptoms associated with diverticulitis, small bowel symptoms, such as partial small bowel obstruction, or associated severe cramps, is frequently the warning sign of a sigmoidointestinal fistula. Consequently, this group of patients demands early surgical resection. Further indications for operation are failure of patients to improve under conservative management or those patients about whom there is a question of the possibility of coexisting carcinoma. While coexisting diverticulitis and carcinoma is rare, often no reliance can be placed upon symptomatology or physical signs in an individual case to differentiate the two diseases. Both appear most commonly in the older age groups and are most frequent in the same segment of colon, and both can produce bleeding, obstruction, and fistula formation. Roentgenologic findings nay be inconclusive as emphasized by Starkloff and Bindbeutal, and sigmoidoscopic examination may not result in a positive diagnosis. Pemberton has stated that approximately 25 per cent of all resected specimens of diverticulitis could not be distinguished from cancer until the bowel had been opened by the pathologist. Since confusion in differential diagnosis of carcinoma and diverticulitis will occasionally persist despite close attention to diagnostic possibilities, therapy should proceed promptly to definitive treatment by sigmoid resection.

TYPE OF OPERATION

Resection should be the ultimate goal in the surgical therapy of complicated diverticulitis. Palliative surgical measures are indicated only to prepare the

patient for resection. Early resection of the involved sigmoid and any adjacent redundant sigmoid should be the procedure of choice. The removal of the redundant sigmoid is important in preventing future stasis and subsequent inflammation in diverticula remaining after resection, because a straight tube which can empty readily is substituted for the redundant bowel in which stasis is prominent. Residual diverticula following resection have not resulted in any recurrent diverticulitis in our experience. When the possibility of coexisting carcinoma is entertained, a complete left hemicolectomy is done with removal of the splenic flexure, division of the inferior mesenteric artery at its point of origin from the aorta, resection of the mesentery of the left colon, and anastomosis between the mid-transverse colon and the rectum at or just below the peritoneal reflection. We do not believe, however, that this operation is indicated as a routine procedure in diverticulitis.

The important aspect of the primary resection and anastomosis is that the anastomosis should be done by the open method using well vascularized bowel without tension. Primary resection without colostomy is the procedure of choice and increasing experience has shown that one stage operations can be done much more frequently than they have been done in the past. Welch and Allen reported that in the past two years 57 per cent of the cases have been done as one stage resections. Two-thirds of our patients have been subjected to one stage operations without mortality. Colostomy is indicated in the patient with complete obstruction in preparation for resection. Diverting colostomy is used in the patient with an inflammatory mass and an associated fistula which does not subside satisfactorily under conservative treatment. In cases of acute perforation with generalized peritonitis, diverting colostomy may be life saving in controlling further peritoneal contamination. Many partial obstructions can be adequately prepared for primary resection without colostomy. Chronic fistulous tracts can also be resected without a primary colostomy. Removal of the diseased sigmoid prevents recurrence of the fistulous tract. Postoperative drainage of the bladder will adequately protect the closure of the fistulous attachment to the bladder. If colostomy is necessary, there appears to be no valid reason for prolonged diversion of the fecal stream prior to resection of the diseased segment. Resection of the sigmoid has followed diverting colostomy in three to six weeks in our patients, depending upon the general condition of each patient. Intraperitoneal closure of the colostomy is then done approximately two weeks after resection. A barium enema is used prior to closure of the colostomy to determine the integrity of the suture line. In any complicated case, concern with regard to the anastomosis at the time of operation can be obviated by the establishment of a complementary colostomy.

Obstructive resection of the Mikulicz type is not advocated because thickening of the pericolic tissues makes mobilization difficult and wide resection of the redundant sigmoid usually cannot be obtained. When proximal colostomy is done because of peritoneal soiling, it should be a truly diverting colostomy. This is best done by completely dividing the bowel. In those patients in whom there is complete obstruction, complete diversion is probably not as necessary, although this has been practiced in our patients. Cecostomy is ill-advised as it does not

adequately divert the fecal stream. If the patient is well prepared for operation and the anastomosis is made without tension and there is a good blood supply, cecostomy would seem to offer very little in the therapy of these patients. When closure of the colostomy is made, it is done by the intraperitoneal method with excision of the ends of the colon and a primary interrupted suture anastomosis.

A further aid in the surgical management of diverticulitis is the use of a long tube of the Cantor type as part of the preoperative preparation for resection. This offers excellent decompression of the small intestine and during the subsequent operation the ease of walling off the decompressed bowel adds to the ease of operation by facilitating exposure.

SUMMARY AND CONCLUSIONS

We have reviewed the trend toward increasingly aggressive treatment of diverticulitis of the colon, as exemplified by good results with low morbidity and mortality rates in many published series of sigmoid resection for diverticulitis. Our experience in a relatively small series confirms the value of excision in contrast to colostomy and other palliative measures.

We believe that the sigmoid should be resected in patients with the following conditions: 1) patients with complications of diverticulitis including perforation, obstruction, hemorrhage and fistula formation, 2) patients in whom there is a possibility of coexisting carcinoma, and 3) patients with recurrent attacks of diverticulitis, and patients with a severe single attack of diverticulitis, particularly if under 50 years of age.

Palliative operations are unsatisfactory. Colostomy, when indicated, may be a life-saving procedure that should be considered merely a step in the preparation of the patient for resection. Excision should include the diseased segment of bowel and the adjacent redundant sigmoid. By broadening the indications for resection and avoiding palliative measures, we believe that the morbidity and mortality rates of diverticular disease of the sigmoid colon can be further reduced.

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NEOMYCIN-NYSTATIN FOR PREOPERATIVE PREPARATION OF THE COLON

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During a systematic investigation of various agents for preoperative preparation of the large bowel[2] one agent has been found to give results which are sufficiently outstanding to warrant a separate report.

The drug combination of Neomycin and Nystatin, in conjunction with the usual mechanical aids to bowel cleansing, has almost completely removed the bacterial flora of the feces. In our hands only one other agent (Tetracycline-Neomycin)[1] has given results which are comparable to those obtained with Neomycin-Nystatin. The results obtained with these two agents warrant different indications for their use. There have been no gastrointestinal reactions severe enough to advise discontinuance of the drug. In our limited experience there have been no other significant side reactions. The therapeutic concentration of the antifungal drug, Nystatin, prevented the overgrowth of yeasts during the period of preoperative bowel preparation and thus obviated some of the difficulties which previously were attributed to yeast overgrowth.

The satisfactory results obtained with this agent make this one of the acceptable methods of preoperative preparation for patients having elective colon surgery on our hospital service.

METHODS

Patients were selected at random from the surgical service. The one requirement was that they not have any known disease of the gastrointestinal tract. They were placed on a low residue diet, given a cathartic the first day of the program, given daily enemas, and received the Neomycin-Nystatin combination according to the following program: Neomycin-Nystatin—2 tablets every hour for 4 hours, then 2 tablets every 4 hours for 72 hours. Each tablet contained 0.5 Gm. of Neomycin sulfate and 125,000 units of Nystatin so that the unit dose was 1 Gm. of Neomycin sulfate and 250,000 units of Nystatin.

Quantitative bacteriologic analyses were conducted on a control stool, stools each day of therapy, and on either the second, third, or fourth day following the discontinuance of drugs. By this means it was possible to evaluate the reduction of bacterial flora in the feces and the rate of return of the flora to its normal level.

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Bacteriologic determinations were conducted by Virginia D. Crane, B.A., M.T. and JoRhea B. Pevey, M.T. (ASCP).

Neomycin-Nystatin was supplied by E. R. Squibb & Sons Division of Olin Mathieson Chemical Corp.

Neomycin-Nystatin is available under the trade name Neomycin-Mycostatin.

Bacteriologic Technics: Bacteriologic technics, outlined in detail previously[2], will be briefly summarized.

One gram of stool was serially diluted with sterile water from 10^2 to 10^{10} dilutions. From each dilution 0.05 ml. were inoculated upon five plates each of: blood agar to be incubated aerobically, blood agar to be incubated anaerobically, and McConkey's agar to be incubated aerobically. After adequate incubation, the colonies were counted and organisms identified through Gram stains, smears, and subcultures. For identification, subcultures were made into brain-heart infusion broth, eosin methylene blue agar, thioglycollate broth, and onto various other media for whatever biochemical reactions or other studies were necessary.

Identification of the various organisms, described in a previous publication[2], followed standard technics.

RESULTS

Five patients were studied. The results, as can be seen from the graphs, indicate that the reduction in fecal flora would justify widespread use of this means of preoperative bowel preparation.

When specimens were not available, no entry was made on the graph. Those entries which indicate no growth indicate the absence of those particular organisms from available stool specimens.

Enterococci and streptococci (fig. 1) were combined for this report although

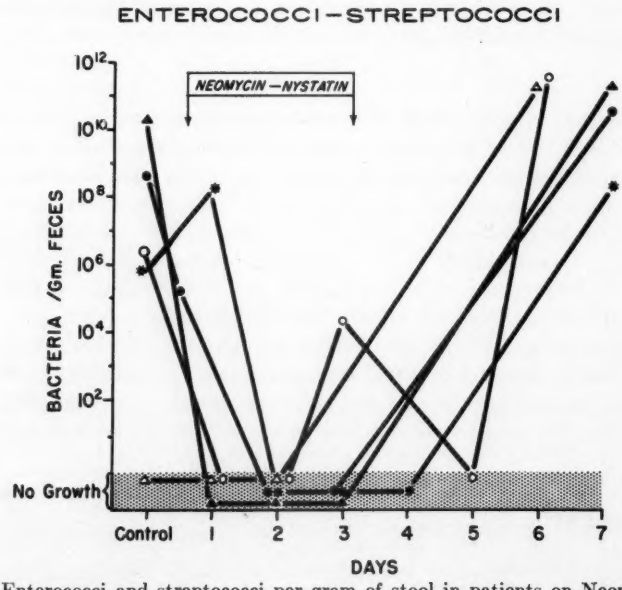

FIG. 1. Enterococci and streptococci per gram of stool in patients on Neomycin-Nystatin for three days. Each symbol represents an individual patient. Symbols are plotted only for days when specimens actually analyzed. Symbols in area of 'No Growth' indicate specimens studied and found not to contain these organisms.

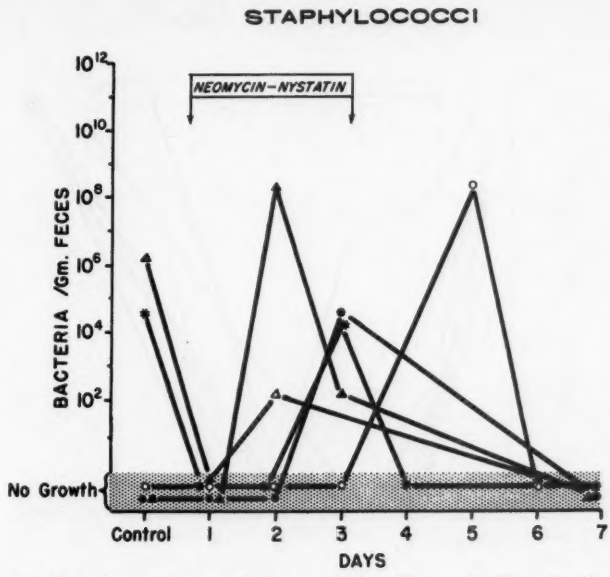

FIG. 2. Staphylococci in feces during and after Neomycin-Nystatin therapy

they were evaluated separately bacteriologically. By the second day of drug therapy they had been eliminated from the feces of all patients and by the end of the third day were detectable only in a single patient. By the third and fourth day following the end of drug therapy, the enterococci and streptococci had returned to or exceeded control concentrations in each of the patients.

Staphylococci (fig. 2) were not present in the control specimens of 3 patients and were absent from the stools of all patients at the end of the first day of therapy. However, on the second and third days of therapy, staphylococci were recovered from 2 and 3 patients. It is interesting to note that the staphylococci did not appear in the feces immediately following the end of drug therapy in any of the patients.

Coliform organisms (fig. 3) were present in all control specimens, but were absent from 4 of the 5 patients by the end of the first day. By the end of the third day of therapy, coliform organisms were absent from the feces of all patients and did not recur again until the second, third, or fourth day following therapy. At this time these organisms returned to their original concentrations or to higher levels.

The absence of clostridia (fig. 4) from the control specimens of all 5 patients is somewhat surprising. Clostridia were present in a concentration of 29×10^2 at the end of the first day in one patient and 1×10^8 three days after the cessation of therapy in this same patient. Clostridia were also found in a concentration of 2×10^6 four days following cessation of therapy in one other patient, but at no other time were clostridia recovered from any of these patients.

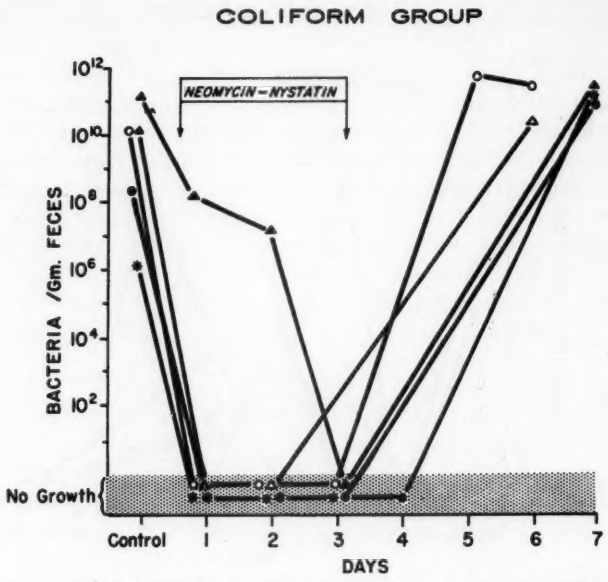

FIG. 3. Effect of Neomycin-Nystatin on coliform organisms in stool

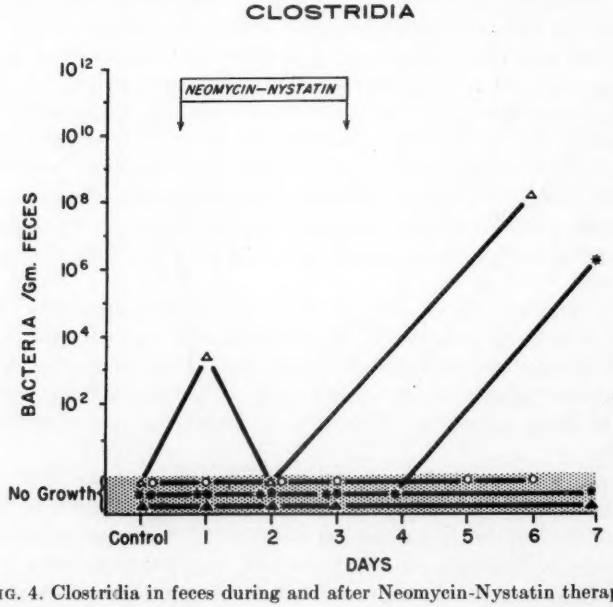

FIG. 4. Clostridia in feces during and after Neomycin-Nystatin therapy

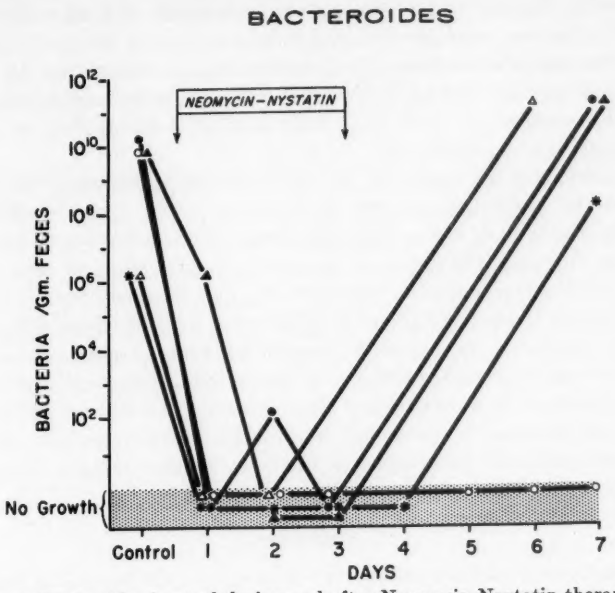

FIG. 5. Bacteroides in stool during and after Neomycin-Nystatin therapy

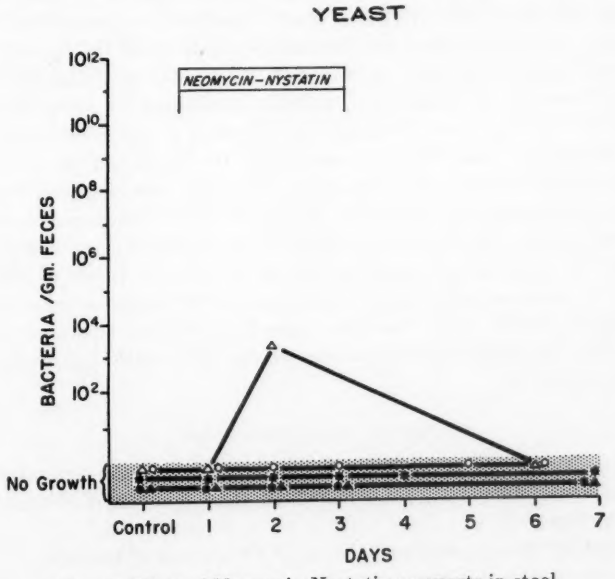

FIG. 6. Effect of Neomycin-Nystatin on yeasts in stool

Bacteroides (fig. 5), which give an excellent index of drug activity against anaerobic organisms, were present in all control specimens, but had been removed from all but one patient at the end of the first day of therapy. By the end of the third day of therapy, the feces of all patients had been cleared of bacteroides. Bacteroides reappeared in at least their original concentration in 4 patients after therapy was discontinued.

The behaviour of the yeasts (fig. 6) was an interesting feature of this study and confirmed the antifungal activity of Nystatin under these conditions. The absence of yeasts from the control specimens was in accord with our previous experience. However, the failure of yeasts to appear *during* and after the period of bowel sterilization indicated effective antifungal drug activity.

Gram positive rods were found in 3 patients, in 2 of whom they were still present at the end of the period of preparation. Proteus species, found in 4 patients, were not recovered at the end of the period of preparation in any. Pseudomonas species were recovered in 2 patients on the last and second to last days of bowel preparation. Lactobacillus was picked up at irregular intervals in 3 patients and anaerobic streptococci in 1 patient. Neither of these were recovered at the end of the period of preparation.

DISCUSSION

The effectiveness of this combination of agents for the control of the bacterial flora of the large bowel in preparation for surgery has been demonstrated by this quantitative bacteriologic study. The rapid and complete disappearance of so many organisms and their relatively rapid return to normal indicate that the drug did not completely upset the normal relationships of the bacterial flora of the gastrointestinal tract but controlled it sufficiently to make surgery safer. Neomycin-Nystatin eliminated the coliform organisms 24 hours sooner than Neomycin alone. There was no significant difference in the response of staphylococci, streptococci, clostridia, or bacteroides to Neomycin or to Neomycin combined with Nystatin. An important difference was observed with yeasts which were suppressed by Neomycin-Nystatin, but which began to proliferate on the second day with Neomycin alone. The control of yeasts suggests that this would be a particularly appropriate agent for two types of patients: 1) those who must have large bowel preparation after being on other antibiotics for a prolonged period, or 2) those who have had sufficient antibiotic therapy to upset the normal bacterial relationships of the colon and thus permit uncontrolled yeast growth.

SUMMARY AND CONCLUSIONS

Neomycin-Nystatin has been studied for preoperative preparation of the large bowel. Quantitative stool cultures evaluated the effects of this combination on the fecal flora.

Three days of therapy rendered the stool almost free of bacteria.

Side reactions were minimal.

Neomycin-Nystatin in combination with mechanical cleansing is one of the

most effective means for preoperative preparation of the colon prior to elective surgery.

Neomycin-Nystatin should be the preferred method of therapy in any patient who has been subjected to prolonged antibiotic therapy prior to colon preparation.

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EARLY AND LATE MANAGEMENT OF CAUSTIC BURNS OF THE ESOPHAGUS*

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INCIDENCE

This report includes a total of 36 patients who were admitted to Parkland Hospital, Children's Medical Center, and to my private practice, since July 1951, with a proved or suspected diagnosis of caustic burns of the esophagus. Some had only burns of the mouth.

Twenty-nine of these patients were seen within a few hours after the burn. Seven were seen three weeks or more after the burn, and all of these 7 had well-formed strictures and progressive dysphagia.

CARE OF THE ACUTE CASE

Caustic burns of the esophagus fortunately are becoming more and more rare in North Texas because home soap-making is being discarded, therefore our experience is not great. However, as this limited experience has gradually increased, a plan of therapy has been evolved, based upon trial and error, advice from the senior members of the Thoracic Surgery and Pediatric Staffs,[15] and upon information gained from literature.

The main points in this plan of therapy are as follows:

1. All patients with acute caustic burns of the mouth, pharynx or esophagus are admitted to the hospital.
2. Broad spectrum antibiotics are given routinely.
3. Gastric lavage is advised with a weak neutralizing solution, if the caustic is known. Under some circumstances, this might be omitted: (a.) In the case of a wildly agitated child, and (b.) if several hours have elapsed since the ingestion.
4. Oral intake is allowed as tolerated, parenteral fluids are given as needed.
5. After 48 to 72 hours to allow for subsidence of the edema of the mouth, careful esophagoscopy and pharyngoscopy are done under general anesthesia, to note the extent of the burns.[5, 18]

If no significant burns are seen on esophagoscopy, then antibiotics usually are continued until all visible swelling is gone and until swallowing is normal, then the patient is discharged. If questionable burns are seen, re-esophagoscopy may be utilized. Barium swallow is not advised until four to five weeks after the initial burn, since strictures rarely, if ever, form prior to 21 days.

If severe burns are seen, it is thought best to leave in place a plastic Levine tube to act as a stent[7].

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ACCURACY OF ESOPHAGOSCOPIC EVALUATION

The question might arise as to whether or not esophagoscopy is an accurate method of evaluating the extent of the burn. Of the 29 patients seen in the acute stage, in 23 of them careful esophagoscopy was done within two to four days after the initial injury. All were done under general anesthesia. There was no morbidity and no mortality. Burns were seen and thought to be severe enough to cause stricture in 3. All of these 3 subsequently developed severe strictures and required therapy. In no instance was a burn severe enough to cause stricture missed at the time of the esophagoscopy. Adequate treatment of any burn would require a knowledge of its extent.

THERAPY FOR THE STRICTURES

On our service all strictures of the esophagus due to caustics are dilated. The method of dilatation and the time to begin dilatations have been the subject of considerable discussion over the years. Bosher, Burford and Ackerman[2] have demonstrated experimentally that there are changes that take place in burned esophageal mucosa in animals which would suggest very strongly that early dilatations are contraindicated. I share this opinion, and therefore believe that the advantages of early dilatations are outweighed by the disadvantages. Their experimental observation that strictures became significant functionally at approximately three weeks after the burn, is borne out by the history and follow-up on the 10 patients in this series who developed strictures. It is now our policy to begin dilatations between three and four weeks after the burn.

Salzer-Bokay Method. Salzer[14] and Bokay[1] have advocated early dilatations beginning a few days after the initial burn. The results that have been reported with this method have been good. I think, however, that the evidence at hand would indicate that early dilatation would require passing the catheter over acutely inflamed mucosa with bacterial invasion, early necrosis, and insufficient time for healing. I would look upon this as undesirable and dangerous and upon the results with considerable skepticism, unless the presence of severe burns have been demonstrated by careful endoscopic examination. It is axiomatic in the treatment of burns anywhere in the body that the best results are obtained when the burns are least severe, and not very serious burns can make any ointment or any method of therapy look pretty good.

Methods of Dilatation. No attempt will be made to review all of the methods. Anyone doing this work has ample opportunity to choose from a wide variety of proven methods, and probably one is almost as good as another, provided gentleness, care and adequate relaxation of the patient are employed. General anesthesia should be used for almost all children and some adults, and it should be deep anesthesia.

Apparently the safest method would appear to be retrograde dilatation through a gastrostomy opening with the Tucker[16] dilators and string. Even though this is the safest method, we do not employ gastrostomy or retrograde dilatations routinely, but, as a matter of fact, have employed this in only those patients in whom a gastrostomy had already been done before the patient was placed on

this program. As a routine, we employ a combination of methods advocated by Jackson[9], Plummer[12], and Vinson[17].

Esophagoscopy is done under general anesthesia, and, with or without the use of an inlying silk thread, the piano-wire dilator guide is passed into the stomach through the stricture and, using the Plummer dilators, the staff and olive are passed down over the wire guide. Extreme care is taken not to tear or split the stricture, not so much because of the danger of perforation as because it is believed that a tear in the stricture delays the ultimate completion of the treatment by six weeks to three months. It is our policy to use only dilators that will pass fairly easily and to increase only two French numbers at each successive dilatation. In each patient a planned program is utilized, beginning with weekly dilatations until the size 39 French olive passes easily three successive weeks, then the time interval is increased.

Nine patients have been subjected to regularly conducted dilatations according to this program. There has not been a death in this group. The only instances of morbidity have been an anesthetic explosion and a nonfatal perforation by the wire. The explosion was due to a defective esophagoscope bulb which was so hot it ignited the expired air-ether combination in a child. All the physicians, nurses and the child survived with only mild injuries. The perforation by wire was recognized and was not followed by dilatation at that time. Mediastinitis did not develop.

Seven of the 9 patients have been completely rehabilitated by this program of dilatation. One had come to us after over a year and a half of sporadic treatment in another institution, and had been fed regularly with gastrostomy. In less than three months, this patient had been dilated until a 39 French dilator passed with ease. He began taking feedings completely by mouth after the first dilatation and has not been fed by gastrostomy since. Such feedings have been taken by the others having dilatations, except 2.

In 2 of the 9 patients, dilatations have been inadequate to completely rehabilitate the patient. One of these has subsequently had an esophageal replacement with a segment of jejunum.* The other is a 3 year old Negro child who has such extensive burns of the entire esophagus, hypopharynx and pharynx that we did not consider a substitution operation because there was no normal tissue above to which to suture the substitute. We therefore dilated this boy at first weekly, and subsequently at less frequent intervals over a period of two years. He is living on oral intake completely, and growing and developing. He does, however, have some pooling of saliva in the pharynx and some aspiration of this saliva at night, and has developed chronic bronchopulmonary disease thought to be on the basis of repeated aspirations.

SELECTION OF PATIENTS FOR DILATATION AND/OR SURGERY

It is the purpose of this paper to re-emphasize the value of a planned program of dilatation for caustic burns of the esophagus. In recent years, Harrison[8], Robertson and Sarjeant[13], Gross[6], Limbacher[11], Buchman and Gay[4], Bosher,

* Done under the direction of Drs. Shaw and Paulson.

Decker and Harrison[3], Javid[10] and others have made outstanding contributions to this field, stressing surgical excision of the strictured areas or substitution operations.

It would appear that there is a middle ground, that some strictures should be dilated, that some should be resected with end to end anastomosis, and that some should be resected with esophageal substitution procedures. We believe that a planned program of adequate dilatations should precede the decision for excisional or replacement surgery.

In some instances, as in our patient mentioned above, the hypopharynx is so badly scarred that the normal peristalsis of deglutition is impossible, and also there is no normal esophagus or hypopharynx above to which to suture a replacement. In this instance, we believe that substitution is ill advised. It is very unusual that a short stricture which lends itself well to end to end anastomosis cannot be easily handled with a planned program of dilatation.

For the extensively burned esophagus, especially if the burn extends through into the muscle coat, substitution may well be advised.

A SUMMARY OF THE FACTORS WHICH FAVOR DILATATION

1. Excellent results with a planned program.
2. No disruption of the normal alimentary tract.
3. No acid or alkaline juices in the upper esophagus or hypopharynx following treatment.
4. Applicable to severe strictures of the hypopharynx and upper esophageal segment and to multiple strictures, where replacement is more difficult.
5. Histologic studies, both experimentally and in resected specimens in humans, reveal that a great majority of the burns involve only the mucosa and the submucosa and it is well known that normal mucosa will grow after careful dilatations.

POINTS IN FAVOR OF SURGICAL THERAPY

1. Present anesthesia, surgical training standards and blood replacement methods make this surgery feasible.
2. Short term therapy.
3. Excellent results in well planned and well executed cases.

CONCLUSIONS

1. Excellent results can be obtained with a planned program of dilatation in stricture of the esophagus due to caustics.
2. Even though multiple procedures and multiple anesthesias are required, dilatation can be done without mortality and with very low morbidity.
3. Excisional and/or replacement surgery should be reserved for patients who can not be rehabilitated with dilatations.

SUMMARY

The incidence of caustic burns of the esophagus in Dallas, Texas and environs has been reviewed.

A plan for the care of the acutely burned esophagus has been presented.

A plan for the care of benign esophageal strictures has been presented, re-emphasizing the value of a planned program of regular dilatations before resection or replacement surgery is advised.

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ESOPHAGEAL PERFORATIONS

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Until recently the management of esophageal perforations has consisted primarily of immediate drainage of the mediastinum at the site of perforation. Although effective in reducing the mortality rate, this approach often has been marked by undesirable features which might be avoided by a more individualized program. We outline a program of selected treatment embodying conservative measures in some instances, and more definitive surgical procedures in others. The advent of newer and safer esophageal surgical technics, and the antibiotics effective against the organisms seen in mediastinitis make such selected treatment possible.

CLASSIFICATION

For purposes of discussion it seemed wise to classify esophageal perforations as follows:

I. Benign—to include

(a) Minute or incomplete mucosal tears from ingested foreign bodies, etc.

(b) Large perforations due to penetrating wounds—trauma from instrumentation, etc.

II. Malignant—to include

(a) Slowly penetrating spontaneous perforations in an extensive carcinoma.

(b) Large perforations of a carcinoma seen following endoscopy and biopsy.

ANATOMY AND PATHOLOGY

Time will not permit of a complete review of the mediastinal anatomy and pathogenesis of mediastinitis. Furstenberg, in 1929, first gave a true clinical analysis of the importance of the mediastinum in the spread of infections within its compartments extending from the retroperitoneal space to the deep fascial planes of the neck, and how frequently one or both pleural spaces may be involved. The anatomic pathways so conducive to a spreading cellulitis are further augmented by the constant alteration of intrathoracic pressures.

Thus in minimal perforations of the esophagus, if untreated, a localized phlegmenous process can extend in all directions within the mediastinum. In large perforations, there will result immediate and continued gross soiling of the mediastinum with air, saliva, and ingested material, and usually one or both pleural spaces will be similarly contaminated.

DIAGNOSIS

The diagnosis of esophageal perforation is not ordinarily difficult, if the possibility is considered. The history is the greatest single factor in leading to the

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suspicion of this condition. Predisposing circumstances such as foreign body ingestion, endoscopy, or penetrating wound should immediately alert one to this possibility. A previous history of dysphagia or violent vomiting could lead to the suspicion of spontaneous perforation.

Three cardinal symptoms almost invariably exist: (1.) Pain with localization at the suspected level of perforation; (2.) Chills and fever, becoming progressively more severe in a matter of hours; and (3.) Dysphagia. Hoarseness may attend the development of glottic edema and this is an ominous sign.

The physical findings will vary, depending on the location and severity of the injury. Signs of mediastinal emphysema with crepitus in the suprasternal notch or a mediastinal crunch may be found. Evidence of pneumothorax should be sought. Upper abdominal tenderness and spasm are common with lower level lesions.

Roentgenologic aids are of course important. Upright films of the chest may show pneumothorax, widening of the mediastinum and contained air, or pleural effusion. Lipiodol visualization often is of great help in the diagnosis. A perforation cannot be ruled out on the basis of a negative lipiodol swallow but it is rare that a large perforation will not be visualized.

TREATMENT

In outlining a plan of therapy, operative or otherwise, certain measures are universally employed, while others will vary from one patient to the next.

Esophageal rest is mandatory and is accomplished by withholding all oral intake. Large doses of penicillin and streptomycin are begun immediately. Beyond this it is our opinion that the treatment should become individualized.

In benign lesions, where only a minimal perforation occurs, provided the patient is seen within the first 12 hours of injury, conservative management with esophageal rest, parenteral fluids, and antibiotics is all that is required. If the injury is due to an ingested foreign body, a careful esophagoscopy should be done. If the foreign body is removed without further laceration of the esophagus, expectant treatment is advised. If evidence of progressive mediastinitis develops under observation, then adequate drainage of the mediastinum must be done, but in our experience this has not been necessary.

In those benign lesions wherein a large perforation has occurred, with severe, early mediastinal emphysema, or a pneumothorax is present, and the defect is visualized with lipiodol or endoscopy, then early operative treatment is called for, rather than a simple drainage procedure. However, we prefer a direct surgical repair of the laceration. This must be done within 24 hours before the resultant acute inflammation renders the tissue unsuitable for suture placement. This direct surgical repair is not only feasible and safe, but is attended with a much lower morbidity as compared with mediastinotomy and the common problem of fistula formation and periesophageal fibrosis.

In perforations of the cervical esophagus, exposure and direct repair is accomplished through an incision along the anterior border of the sternocleidomastoid

muscle extended down medial to the carotid sheath and lateral to the trachea and thyroid gland. At lower levels, a transpleural approach affords excellent exposure for freshening of the lacerated edges and direct suture repair in layers. It also presents an unexcelled opportunity to remove any retained foreign body, or manage any concomitantly existing pleuro-pulmonary pathology resulting from the perforation. In contrast to this approach to early perforations is the surgical management of frank mediastinal suppuration seen in late cases. The latter problems no longer present any opportunity for primary repair and no course other than drainage can or should be employed.

In those cases wherein malignancy is the underlying cause for the perforation, the management is based on different reasoning. Spontaneous perforations of a malignancy will not heal of their own accord. However, extensive mediastinal sepsis is unusual in these patients because of the slowly penetrating nature of the perforation with adequate sealing off of the adjacent mediastinum with tumor and fibrosis. An accasional such patient will present need for drainage of a localized mediastinal abscess. Spontaneous perforation of an esophageal carcinoma is conclusive evidence of nonresectability, and in our opinion a feeding gastrostomy should be done.

An entirely different attitude should be held regarding perforation of a neoplasm as a result of endoscopy or biopsy. Such an accident may well occur in a lesion which is still resectable. If conservative management and mediastinotomy alone are employed in such instances, the resulting fibrosis and inflammation adjacent to the carcinoma will preclude resection at a later date. Therefore, in our opinion it is imperative that such a patient be treated by primary resection of the perforated neoplasm within as short a period of time as is feasible after such an accident occurs. Under these circumstances the perforation and mediastinitis can be disregarded and the patient treated as any other elective esophageal resection.

If the perforated lesion at the time of thoracotomy is found to have exceeded the limits of resectability because of its extensive nature, then an attempt should be made to close the perforation with a pleural graft or other suitable adjacent tissue, and drainage should be provided in case of further leakage. In such hopeless patients a feeding gastrostomy should be done either at the same time or within a day or two to rest the esophagus permanently and provide an avenue for alimentation.

SUMMARY

In summary we would emphasize a need for more thorough evaluation of esophageal perforations which will permit of more selective and individualized treatment. Whereas the policy of routine early drainage of all esophageal perforations has served to reduce the mortality rate in such patients, we are convinced that present surgical technics and intelligent antibiotic therapy as outlined will significantly reduce the morbidity as well as the mortality rates in these patients. By no means do we wish to dispute the urgent, life saving need for mediastinal drainage in well established suppurative mediastinitis. It is our

belief that such mediastinitis and its sequelae can be avoided in many instances by either conservative measures in the case of minor injuries, or by direct surgical repair in the more extensive lacerations, when seen early. Finally, we would emphasize the need for immediate surgical removal of the malignant lesion with instrumental perforation, in order that all hope of eventual resection will not be lost.

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THE TREATMENT OF PREOPERATIVE AND POSTOPERATIVE STRESS

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The care of the surgical patient has improved in the past 15 years with the introduction of intratracheal anesthesia, the sulphonamides and antibiotics. Early ambulation shortens the hospital stay and the replacement of blood loss has been facilitated by the introduction of blood banks. Preoperative blood and vitamins, B complex and ascorbic acid, in intravenous fluids has been thought to aid in wound healing, but disruption continues to occur in the protein depleted patient.

Maintaining adequate blood pressure during the operative and immediate postoperative period prevents the cerebral and renal shutdown that often proves disastrous.

Gas pains and the often fatal and unrecognized acute gastric dilatation become rare occurrences when the postoperative patient is promptly and briefly supported in a sitting position to facilitate the expulsion of swallowed air, thereby maintaining vasomotor tone.

Perhaps we have gone too far in the routine use of sulphonamides and/or antibiotics postoperatively. Absolute asepsis, complete hemostasis, gentle handling of tissues and careful approximation of tissues remain the cardinal surgical principles. With the routine use of antibiotics the patient may have been discharged before postantibiotic infection develops or the distressing and dangerous allergic reaction to antibiotic therapy appears. When and if infection occurs it appears three to five days postoperatively and can be treated by massive doses of antibiotics for several days. Allergic manifestations usually may be minimized with administration of an antihistaminic along with the antibiotics.

The anticipation of an operation in certain patients may produce a stress syndrome as severe as that from the actual operation and can lead to prolonged convalescence. Fright stimulates the adrenal medulla; the pituitary, adrenal cortex, and thyroid then are called upon and if these glands are not protected by adequate protein, ascorbic acid and proper steroids they become depleted. Overactivity of the sympathetic nervous system in fright can lead to exhaustion and a lowered threshold for pain.

Such a reaction to fright also occurs from an operation and attempts have been made to block the sympathetic chain at operation and thus prevent its overactivity and the depletion of stimulated endocrine glands. Others have tried to anticipate the effects of stress on the cellular chemicals and on the endocrine glands, mainly the pituitary and adrenal cortex, by giving physio-chemical and hormonal replacements before and immediately after operation.

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René Leriche in 1933 before the French Congress of Surgery developed the concept of the postoperative disease in considering the delayed effects of operation.[4] In this postoperative disease the clinical and biologic changes after operation did not involve the condition for which the operation was done nor involve infection or a technical fault. He considers the local effects as comparatively unimportant and the general reaction as dominating the picture. These general reactions involve, (1) a humoral syndrome, (2) a vasomotor syndrome, (3) a blood and leukocytic reaction and (4) a hormonal syndrome. In 1937 he gave priority to the vasomotor syndrome believing that the clinical and biologic manifestations of the postoperative disease have the same cause, namely, the original injury to the autonomic system. In proportion to the violence of aggression which may be reduced by gentleness and respect of tissue life he believed that *"not only every patient, but also every surgeon, has his own postoperative disease"*.

Leriche[5] now believes that to avoid the operative disease it is useful, or even necessary, to block both the centripetal stimuli at the site of operation and the centrifugal responses, that is to say autonomic responses, which cause imbalance at the periphery. This can be done in two ways: either by drugs having a general action, ganglioplegic drugs, with or without refrigeration, or by procaine infiltration of sensory nerves and vessels together with a paravertebral block of the sympathetic chain. The first method is simple but perhaps not safer as it does more than is strictly necessary. The second has the drawback of taking time and skill but probably is the better of the two.

Corelli[2], in discussing the quantitative and qualitative blood changes after surgery, points out that since the work of Selye an operation can be thought of as an *"acute agression"* with hormonal, nervous and autonomic reactions and provoking adrenocortical stimuli and the adaptation syndrome. The postoperative chemical findings indicate a fall in blood chlorides and increase in adrenocortical activity. The blood potassium falls slightly and the calcium level rises temporarily, then falls. In the first few postoperative days the blood nitrogen rises, then falls. Albumin generally rises because of a rise in globulin. The leukocytes are increased slightly but the eosinophils fall and when these rise in number it indicates a good prognosis.

Abbott,[1] after investigation of 200 patients, discusses the general nutritional needs of the surgical patient, believing that nitrogen given intravenously in the form of improved protein hydrolysates can be utilized by the postoperative patient. The wasting of protein and body tissue can be minimized providing the mineral and vitamin deficits are restored to near normal and the patient received both adequate nitrogen and calories. His studies indicate that the use of hypertonic carbohydrate solution (10 to 20 per cent) and probably carbohydrate and alcohol solution cause a greater sparing of nitrogen than do the available intravenously administered fat emulsions. In attempts to further diminish the loss of weight and nitrogen in the postoperative period the newer longer acting derivatives of testosterone propionate (nortestonate) have been found to maintain weight and to conserve nitrogen.

Protein deficiency leads to acute manifestations such as shock, lowered re-

sistance and slow healing. Dubos[3] and others, at a meeting of the Royal Society of Medicine in April 1955, described experiments that would increase the susceptibility of mice to infection. The most effective way of lowering resistance is to starve the animal for 48 hours before inoculation. If mice are fed synthetic diets containing amino acids in place of protein their susceptibility to infection is increased tenfold, but if whole protein is added normal resistance is restored, although not all proteins are equally effective in this respect. The findings in mice also suggests that the sugar-vitamin-aminoacid mixtures so commonly given to patients in emergency situations may not be the best for restoring resistance.

F. D. Moore[6] in his E. D. Churchill lecture in 1952 has discussed bodily changes in surgical convalescence which are brought up to date in the 1954 annual report on Stress. He considers four phases of convalescence:

I. The adrenergic-corticoid phase
II. The Corticoid withdrawal phase
III. The spontaneous anabolic phase
IV. The fat gain phase

Phase I lasts from one to three to five days. There is increased secretion from the adrenal medulla with a rise in pulse rate, vasoconstriction and elevated blood sugar. The patient is listless, inactive, has no hunger, and there is a relative oliguria. A deranged metabolism is indicated by increased nitrogen and potassium excretion. The end of this phase is determined by returning peristalsis with flatus.

Phase II extends from about the fourth to the sixth or seventh day. The patient is *"ambitious but weak"*. There is water diuresis and the wound is free of pain. Nitrogen and potassium excretion is decreased and sodium increased. When there is a marked increase in eosinophils Phase III is at hand provided the diet is resumed.

Phase III extends from the seventh to about the tenth day. Increasing strength is noted, the patient is hungry, ambitious and strong. Sexual function is not vigorous. A sustained positive nitrogen balance begins. Blood chemistry and urinary output is normal.

Phase IV begins about the second week and may extend up to the eighth week. There is gain in weight and return of sexual activity.

This outline of the bodily changes in convalescence as presented by Moore, Leriche, Corelli and others offers an opportunity to neutralize these chemical, endocrinological and sympathetic alterations by appropriate and timely substitution and thereby shorten convalescence.

This shortening of convalescence we have obtained by instituting the following procedures which seem more rational than letting *"nature run its course"*.

On the day of operation intravenous glucose in saline solution containing vitamin B complex and 500 mg. of ascorbic acid usually is given. As the vitamin B complex and ascorbic acid pull the minerals from the cells, potassium and calcium, at least, should be given for replacement.

If the patient gives a history of bruising easily, 10 to 80 mg. of vitamin K subcutaneously are given just before operation.

Patients depleted in protein receive an injection of the long acting testosterone

propionate or this can be given sublingually, 5 mg. of testosterone twice daily for three or four days. Intravenous protein hydrolysate may be given daily for two or three days until the patient can take the high protein diet.

On return from the operating room, although still not fully recovered from the anesthetic, the patient is supported sitting on the side of the bed and the back tapped repeatedly to expel the swallowed air from the stomach as no amount of suction on the operating table will remove this air. This "*burping*" is repeated every two hours for two or three times the day of operation in order to minimize the development of gas pains and acute gastric dilatation. Daily, from the day of operation, the patient is early ambulated to maintain vasomotor tone.

Within six hours after operation the patient receives by mouth or gastric or jejunal tube[7] if present, 1 teaspoonful of Elixir Triple Potassium (Squibb) and 1 tablespoonful of Syrup of Neocalglucon (Sandoz) for replacement of calcium. This is repeated one to three times daily for the first three or four days dependent on the amount of adrenal cortex required by injection for control of pain.

The rational procedure for the relief of pain is to raise the threshold of pain by giving subcutaneously 0.5 cc. of adrenal cortex extract (Upjohn) every one to three hours postoperatively p.r.n. Occasionally codeine grains one-half are added. Since the adrenal cortex administered will also pull potassium and minerals from the tissues, for every 1 cc. of the injectable cortex given, a teaspoonful of triple potassium and a tablespoonful of neocalglucon are given by mouth. After the second or third day the patient can suck a cortalex tablet (Upjohn), which is the dried adrenal cortex, and after this preparation the potassium and calcium also must be used.

Seconal grains three-quarter is ordered p.r.n. every three hours as necessary for rest or sleep.

For excessive perspiration or emotional disturbance, indicative of anterior pituitary exhaustion, Elixir Reserpoid (Upjohn) 1 teaspoonful is given daily for several days. This alkaloid reserpine from the rauwolfia root suppresses the activity of the hypothalamus which has been stimulating the anterior pituitary.

By employing the adrenal cortex extract for pain, maintainence of the cortex to near normal is insured so that the listlessness and tiredness of the patient is quickly overcome.

With this procedure Phase I of Moore lasts one to two days and Phase II another two days and Phase III is usually over by the end of a week.

Patients who have been stressed by long standing pain from tumor or nerve pain have depleted endocrine glands, particularly the adrenal cortex and anterior pituitary and, secondarily, the thyroid and gonads. These patients return home with a preparation of vitamins and minerals such as Viterra (Roerig) or Paragan M (Squibb), with additional 100 mg. tablets of ascorbic acid and Pancreatin and Bile (Armour) or Desicol (Parke Davis) to aid in the absorption of the vitamins and the mineral combination. These preparations are given daily before a meal and either a cortalex tablet is sucked or a Suprarenal cortex, three grain tablet (Armour) is taken. For exhaustion during the day one or more cortalex tablets are sucked and potassium chloride (15 grains) and multimineral tablets (Stayner)

are taken to counterbalance cellular depletion of potassium and minerals. For perspiration or crying tendency a five grain anterior pituitary tablet (Parke Davis) is sucked as necessary with protection by potassium and multimineral tablets until the reserpoid, 0.25 mg., or reserpine taken simultaneously has stopped the excessive perspiration. The nasal congestion usually accompanying reserpine administration is largely overcome if propadrine, 50 mg. (Sharp and Dohme) is given along with the drug.

When indicated, desiccated thyroid, grains one-quarter, dissolved in the buccal mucosa, is given. The dosage is adjusted to the individual needs of each case with the full understanding and cooperation of the patient. A lag in acuity during normal activity signals the onset of fatigue indicating the need of minute (grains one-quarter) doses of thyroid retained in the mouth and 1 to 5 drops of organic iodine, such as Wampole's Organidin, in water.

For depleted gonads, linguets of estradiol and testosterone in proportions of about 1 to 20 can be used daily for one to two weeks, then every other day for a month. Di-met (Organon) or Femandren (Ciba) are available in about the right proportions.

SUMMARY

The bodily changes in surgical convalescence as presented by Leriche, Moore and Corelli offer an opportunity to neutralize these chemical, endocrinological and sympathetic alterations by appropriate and timely substitution and thereby shorten convalescence.

A detailed description is given of the application of chemical and hormonal therapy preoperatively and postoperatively with a supportive regime whenever necessary on or after discharge from the hospital.

This more rational postoperative therapy has shortened convalescent periods by a week, more or less, as compared to Moore's outline and leaves the patient in a more adequate bodily balance.

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DIVERTICULOSIS OF THE JEJUNUM

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The dramatic advances in medical knowledge have to a degree lessened the interest in some clinical entities. Nevertheless, the many organic lesions that defy accurate diagnosis and satisfactory therapy should frequently be reviewed to alert one to their possible presence. Jejunal diverticulosis belongs in this category. The lesion is not new and probably has uncommonly been present since before the dawn of medical history.

INCIDENCE

Fischer[7] in 1900 stated that one of the earliest reports of this uncommon lesion was that of Sommering in 1794. Sir Astley Cooper[5] in 1844 described 50 diverticula in a postmortem examination of a man who died of *'dropsy'*. Sir William Osler[15] counted 53 diverticula in an autopsy of a man aged 65 years. Four hundred diverticula were reported in a case of Hansemann,[11] but apparently were the total for the entire intestinal tract. Fraser[8] listed 1 in 5000 cases at the Royal Victoria Hospital. Gordiner and Sampsin[10] studied the records from various hospitals and found 16 cases reported in 14,068 autopsies. Case[3], in 6,847 complete barium meal studies, diagnosed diverticulosis of the jejunum in 4 instances, and of the jejunum and ileum in 1. His roentgenologic diagnoses were not all verified by surgery or postmortem examination. Edwards[6] carefully examined 881 autopsy specimens and found 5 cases, and Benson and associates[1] reported 122 cases from the records of the Mayo Clinic. Twenty-one cases is the total listed in the records of The New York Hospital (table I). It is probable that the incidence is somewhat higher in the general adult population than the reports indicate, as the diagnosis can tentatively be made by roentgenographic examination and verified only by surgery or autopsy.

ETIOLOGY

The factors in the causation of diverticula are not completely understood. The lesion occurs along the mesenteric border of the jejunum and rarely in the first part of the ileum. Lewis and Thyng[14] stated that knob-like intestinal diverticula occur regularly in the embryos of the pig, rabbit and man. They regress and are not present in infants and children. Ladd and Gross[13] do not report the lesion occurring in the early years of life.

Klebs[12] probably was the first to advance the theory that the lesion resulted from a fibrous tissue deficiency in the bowel wall at the site of entrance of the blood vessels. Edwards[6] studied the problem, and made anatomic dissections of the small bowel further substantiating Klebs' concept. In long-standing in-

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TABLE I

Summary of cases of jejunal diverticulosis seen at the New York Hospital

Case, Age, Sex	Symptoms	Clinical Diagnosis	Roentgenologic Diagnosis	Operation and Findings
1, 65, M	Flatulence	Diverticulum of jejunum	Diverticulum of jejunum	Adhesions; diverticulum resected
2, 54, M	Tarry stools, flatulence, pain	Marginal ulcer; diverticulosis of stomach	Diverticulum of jejunum; marginal ulcer of jejunum	No operation
3, 20, M	Tarry stools, pain	Marginal ulcer	Marginal ulcer of jejunum	Resection of stomach; small diverticulum present—not resected
4, 72, F	Melena, hematemesis, flatulence, pain	Diverticulosis of duodenum and jejunum	Diverticulosis of duodenum and jejunum	Resection of diverticulum; diverticula persisted
5, 56, F	Flatulence, pain, tarry stools	Diverticulosis of jejunum	Diverticula of jejunum	No diverticula found
6, 54, M	Pain, flatulence, tarry stools	Peptic ulcer	Diverticulosis of duodenum and jejunum; cholelithiasis	No operation
7, 63, F	Flatulence, pain	Intestinal obstruction; incarcerated hernia	Intestinal obstruction due to incarcerated hernia	Multiple jejunal diverticula, no resection (see text)
8, 49, M	Tarry stools, indigestion	Peptic ulcer	Hiatus hernia; peptic ulcer; diverticulosis of small bowel	Resection of stomach for ulcer; diverticulum left. Multiple diverticula found—not resected
9, 80, M	Flatulence, pain	Carcinoma of stomach	Diverticulosis of jejunum	No carcinoma of stomach; resection of diverticulum
10, 50, F	Flatulence, vomiting	High intestinal obstruction	Intestinal obstruction	Gastroenterostomy; resection of diverticulum
11, 40, F	No symptoms	Admitted for varicose veins	Diverticula of duodenum and jejunum	Varicose veins only
12, 57, M	Hematemesis, tarry stools	Peptic ulcer-bleeding; diverticulum of jejunum	Duodenal ulcer; diverticulum of jejunum	Resection of stomach and jejunal diverticulum
13, 60, F	Flatulence, pain	Ventral hernia; hiatus hernia; cholelithiasis	Hiatus hernia; diverticulosis of duodenum and jejunum	Choledochotomy; diverticulum not noted
14, 63, F	Pain	Duodenal ulcer; obstruction of pylorus	Duodenal ulcer; diverticula of colon	Subtotal gastrectomy; jejunal diverticula incidentally found—two resected; several left
15, 43, F	Melena	Carcinoma of descending colon; jejunal diverticulum	Jejunal diverticulum	Resection of colon; diverticulum not noted
16, 81, F	Weakness	Malnutrition; diverticulosis of colon and small bowel	Diverticulosis of colon and small bowel	None
17, 75, F	Pain, indigestion	Carcinoma of colon	Diverticula of jejunum	Excision of polyp of sigmoid; resection of 2 ft. of jejnum for diverticula

TABLE I (*Continued*)

Case, Age, Sex	Symptoms	Clinical Diagnosis	Roentenolgogic Diagnosis	Operation and Findings
18, 53, F	Pain, vomiting	Duodenal ulcer; pyloric obstruction	Duodenal ulcer; diverticulum of duodenum and jejunum	Subtotal gastrectomy; no diverticulum found
19, 50, F	Flatulence, vomiting	Intestinal obstruction; malformed jejunum; multiple diverticula small bowel	Negative findings	Multiple jejunal diverticula; resection of involved segment
20, 40, F	Indigestion, anemia	Diverticulum of ileum	Single jejunal diverticulum or reduplication of small bowel	None
21, 65, F	Pain	Appendiceal abscess; diverticulum of small bowel	Barium enema only—negative	Appendiceal abscess; numerous diverticula of jejunum and ileum—not resected

testinal obstruction surgeons have repeatedly observed that the peritoneum covering the bowel splits first on the antemesenteric border, the site where the circulation is first compromised. When this occurs it is known not to give rise to diverticula. Chlumsky[4] several years ago showed experimentally that by distending the small intestine of living dogs, rupture occurred on the antemesenteric border; whereas by distending the small bowel removed from the dog 10 hours after death, rupture took place along the mesenteric attachment. No normal intrajejunal tension approaches the pressure present in acute intestinal obstruction.

Diverticula are found in adult life. In the 21 cases reviewed here the ages of the patients varied from 20 to 81 years, the average being 59 (table I). Some reports suggest that the lesion is more common in men than women. In this group there were 8 men and 13 women. Their presence in the mature years only is evidence that they are acquired lesions.

PATHOLOGY

The lesion usually is multiple, although only one may be present. They are limited to the jejunum and rarely found along the first part of the ileum. Like those in the colon they are herniations of the mucosa and submucosa through the muscular layers of the bowel wall. At times the wall of a diverticulum may contain a fragment of muscle. A moderate amount of hypertrophied muscle is sometimes found at the base. In the majority of instances the wall consists of serosa, submucosa and mucosa.

The smallest diverticula lie aside the mesenteric angle, the largest bestride the angle. They vary widely in size, measuring 0.5 cm. in diameter to 10 to 12 cm. Those with the greatest diameter, and sometimes the smallest ones, become congested and present evidence of chronic inflammation. When several large ones are present the intestinal wall becomes chronically thickened, bluish-red

in color, and edematous. While the lumen of the bowel is not encroached upon by the diverticula, the contents, when large, may not empty readily and, coupled with diverticulitis, distorts and kinks the intestine thereby compromising the intestinal lumen, which results in varying degrees of obstruction. The diverticulitis may be so severe as to result in perforation and peritonitis[15].

DIAGNOSIS

There are no symptoms or signs characteristic of this condition. Vague recurring abdominal pain, flatulence and loss of appetite may be present. In the more severe cases flatulence progresses to marked distention and the patient is able to pass only small quantities of gas. There is complete loss of appetite and nausea and vomiting may ensue. A roentgenogram plate of the abdomen usually shows fluid pockets not always distinctive of diverticula. Barium enema studies may outline pockets in which there remains residual barium. The following case is reported to illustrate the lesion and the problems in diagnosis and therapy it presents:

CASE REPORT

A white woman was 49 years of age when first admitted to the New York Hospital Dec. 9, 1939. Her chief complaint was abdominal distress and inability to move the bowels, but was able to pass small quantities of gas. She also was suffering from pansinusitis. Her abdominal complaints had been recurrently present for several years but were always relieved by enemas and colonic irrigations. She had never been subjected to surgery. The remainder of her history was noncontributory. *The pertinent physical findings* were that of an acutely ill white woman, tall of stature and weighing 42 kg. There was pronounced abdominal distention with borborygami present. A flat roentgenogram of the abdomen showed "large amounts of gas present." A barium enema was reported as "negative for any abnormality." A gastrointestinal roentgenographic series was not done. She was treated conservatively with enemas and discharged improved on Dec. 29, 1939.

On Sept. 23, 1947, approximately eight years later, she was readmitted to The New York Hospital complaining of severe abdominal pain, distention and inability to evacuate the bowels. During the intervening years she had been relatively well except for recurring bouts of abdominal pain and distention. These episodes had been relieved by enemas and colonic irrigations. There had been loss of appetite and further loss of weight. There had been no nausea and vomiting. *The positive* physical findings showed a thin, emaciated, acutely ill woman with marked abdominal distention. Proctoscopic examination showed no abnormalities and a barium enema was reported as "excess gas in the bowel." A gastrointestinal roentgenographic series showed "segmental dilatation of the jejunum without evidence of obstruction." The esophagus, stomach and duodenum were reported as normal, "without interference to passage of barium." Other studies were unrevealing. She was treated conservatively and discharged improved on Sept. 29, 1947.

She was admitted to The New York Hospital for the third time on July 5, 1953, at which time she came under the writer's observation. Her chief complaint was the same as on the two previous admissions. The episodes of abdominal pain and distention had become more frequent and severe and increasingly difficult to control. She had lost more weight and complained, for the first time, of ankle edema. There had been loss of appetite, nausea and vomiting. *On physical examination* the patient showed marked emaciation, with dry skin almost devoid of any subcutaneous fat. The abdomen was much distended and there was 4 plus ankle edema. She was unable to pass either feces or gas. Conservative measures were instituted with partial relief of the obstruction. Four days after admission a gastrointestinal

roentgenographic series was done which was reported as "ptosis of stomach; partial bowel obstruction which may be due to incarceration of a hernia." An roentgenogram taken 24 hours later was reported "residual barium in small bowel suggests partial obstruction possibly due to inguinal hernia" (figs. 1a, 1b; 2a, 2b). *In the repeated physical examinations the patient had never presented evidence of any external hernia.* Three days later another roentgenogram showed "no retained barium, no evidence of obstruction." Other studies were made with the following results: Proctoscopic examination was negative. The hemoglobin was 9 Gm., the red blood cells were 3,600,000 per cu. mm., the white blood cells were 8,700 per cu. mm. with polymorphonuclears 64 per cent; the urinalysis was normal; the gastric analysis showed free hydrochloric acid of 92 and a total of 112, the serum protein on three tests averaged 5.1 with an albumin-globulin ratio of 3.8 to 1.3; the blood sugar was 74, the urea nitrogen was 21, the alkaline phosphatase was 2.4, the sodium was 140. With the tentative diagnosis of an incarcerated internal hernia causing the recurring intestinal obstruction, operation was recommended even thought the patient's condition was not favorable for surgical intervention.

She was operated upon on July 16, 1953. Through a left rectus incision the peritoneal cavity was entered. There was no evidence of excess fluid and no blood. The entire jejunum and upper ileum were distended, edematous and bluish-red in color. Numerous large and small diverticula were present along the mesenteric border of the entire jejunum (fig. 3a, 3b). The largest ones were located bestride the mesenteric angle, the smallest ones aside the angle. They varied in size from 0.5 to 12 cm. in diameter. An accurate count was not made but there were 15 to 20 large and innumerable small ones. They were present from the ligament of Treitz to the ileum. None was present on the antimesenteric border.

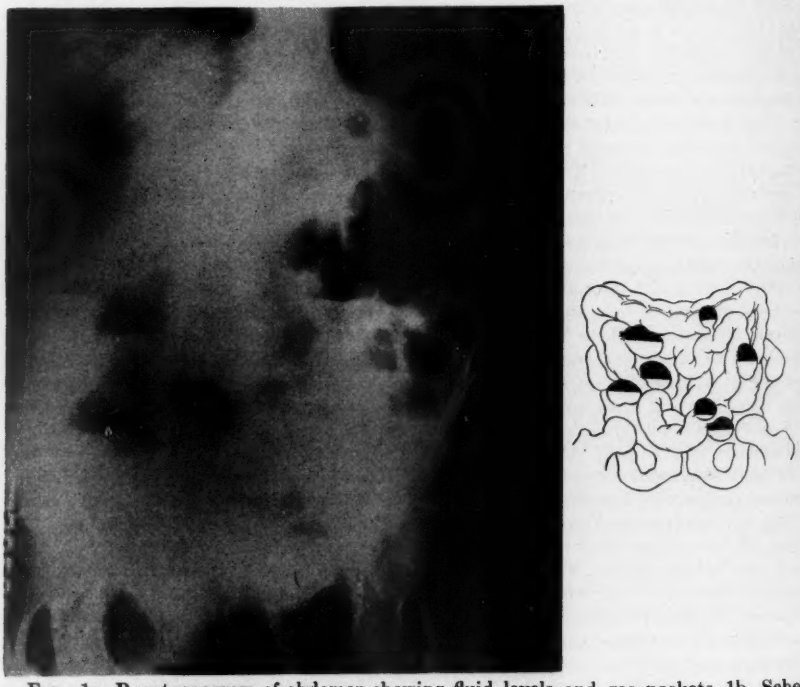
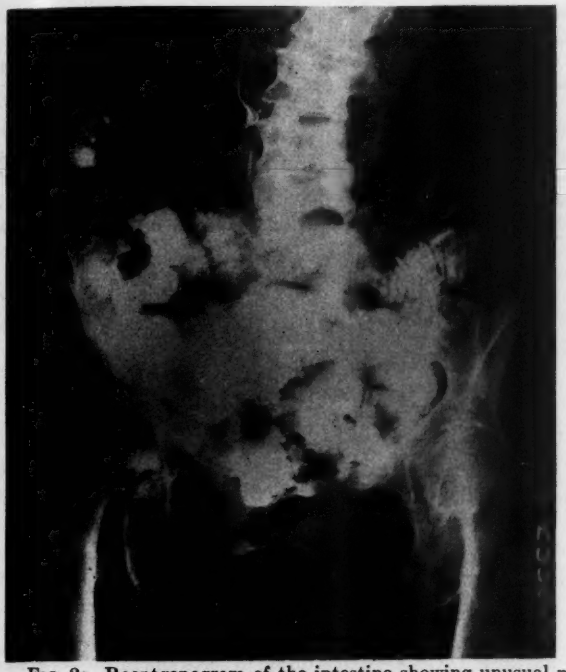


FIG. 1a. Roentgenogram of abdomen showing fluid levels and gas pockets. 1b. Schematic line drawing of the isolated pockets.



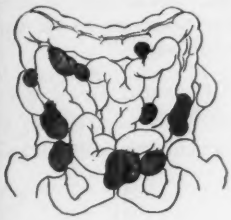


FIG. 2a. Roentgenogram of the intestine showing unusual pattern of barium shadows. Note the one behind the head of the right femur. 2b. Schematic line drawing of the roentgenographic plate based upon the operative findings. Many more diverticula than shown were present.

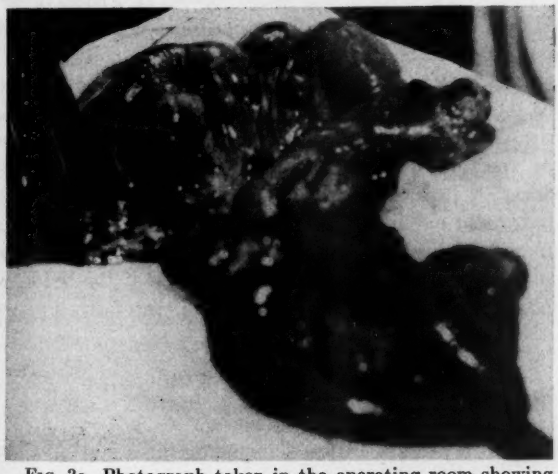


FIG. 3a. Photograph taken in the operating room showing a small section of jejunum and a few of the diverticula. 3b. Schematic drawing of the photograph which illustrates vividly the size of the lesions.

While the technical problem was surmountable, it was obvious that to include all the lesions the entire jejunum would have to be sacrificed. It finally was decided that the patient's condition would not withstand physiologic insult of such magnitude. Accordingly the incision was closed and the patient returned to her bed. She was discharged improved on July 29, 1953.

She was observed at subsequent intervals with recurring episodes of moderate obstruction which were relieved by enemas. Her problem became so acute that she was readmitted for the fourth time on Jan. 3, 1955. There had been further loss of weight, severe abdominal pain, loss of appetite and distention. There followed prompt improvement with conservative measures. She was discharged on January 19, 1955. The necessity of further treatment is anticipated.

Comment. In all cases of recurrent intestinal obstruction, even though scars of previous surgery are evident, jejunal diverticulosis should be considered as a cause in the differential diagnosis.

TREATMENT

The lesions may be present without causing symptoms. When they are responsible for the patient's illness and dominate the pathologic scene, ideally the involved segment of intestine should be resected. A diverticulum which is large and with a narrow neck can be excised with closure of the bowel at the site. Inversion would tend to block the intestinal lumen. If the neck is wide, excision as opposed to resection may compromise the circulation of the localized section of bowel and gangrene of the part result. Furthermore, other diverticula may develop subsequently[2, 9].

In the 21 cases reviewed (table I), 16 were diagnosed diverticula of the jejunum by roentgenologic study, 8 were resected when found at operation and 4 were not resected, other pathology dominating the scene. Four patients were operated upon and no diverticula found, and in 4 there was no operation. In 2 cases diverticula were not suspected but were present and responsible for the patient's symptoms. There were no postoperative deaths.

There is a difference of opinion as to how much of the small intestine may be sacrificed with survival of the patient. Boling[2] resected 153 cm. with survival. In the older age group with debility and malnutrition, extensive resection does not seem justifiable. With resection of an inadequate part, diverticula may remain and the problem persist[2, 9]. In the case herein detailed, in our opinion, the extensive resection required would not have resulted in survival of the patient. The decision to resect must be individualized according to the extent of the disease and the amount of intestine to be sacrificed. Persistence of the lesion is compatible with satisfactory health, provided the patient carefully follows physiologic habits.

SUMMARY

The historic aspects of jejunal diverticulosis are reviewed.

The presence of the lesion as a possible cause of recurring intestinal obstruction should be considered in the differential diagnosis.

The etiology and pathology of the lesion are discussed.

The problem in treatment is outlined.

A case is presented to illustrate some of the various problems the lesion presents.

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DIVERTICULOSIS OF THE JEJUNUM: REPORT OF A CASE SIMULATING GASTRIC CARCINOMA

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The first report of jejunal diverticula was made by Sir Astley Cooper[15] in 1844 of a case found at autopsy. From that time until 1938, only 187 cases were reported[6] and, since then, there have been only sporadic additional case reports. Martin and associates[13] concluded that the incidence of acquired jejunal diverticula in the general population is about 0.5 per cent. Gordinier and Sampson,[8] in 1906, were the first to report seeing these lesions at operation. They reported a case of partial intestinal obstruction due to jejunal diverticulitis which was cured by resection of the narrowed segment of the involved bowel.

In 1920, Case[4] made the first roentgenologic diagnosis of this entity. In 1939, Weber[25] stated that he believed that jejunal diverticula could be diagnosed most of the time by air-contrast studies of the small bowel, but Paul F. Fox and co-authors[7] pointed out the unreliability of barium roentgenograms in that known jejunal diverticula, found at exploratory celiotomy, often fail to fill up with barium. In 122 cases of jejunal diverticulitis seen at the Mayo Clinic between the years 1909 and 1942 inclusive, 85 cases were diagnosed at autopsy, 21 at abdominal exploration, and only 16 by roentgenologic studies.[2]

The etiology of jejunal diverticula is still being debated and will not be discussed in this report.

The most common site for diverticula of the alimentary tract is the colon with the ileum (Meckel's diverticulum), duodenum, pharynx and esophagus, stomach and jejunum following in frequency in the order stated.[7, 9] In the jejunum most of the diverticula are near the ligament of Treitz and diminish distally in size and number.

SYMPTOMS AND DIAGNOSIS

According to most authors, uncomplicated jejunal diverticulosis is rarely associated with symptoms. When present, the primary reported symptom is "*flatulent dyspepsia*". Rosedale,[21] however, reported in 1935 that occasionally a patient may have abdominal pain 1 to 3 hours after eating, nausea, vomiting, abdominal distention, and borborygmus relieved by changes in body position, and constipation. Braithwaite,[3] in 1923, reported the history of a patient who had a fecal taste associated with vomiting. Rose,[20] in 1953, reported 7 cases of patients who had multiple diverticula of the jejunum and ileum in whom he made a differentiation of the two locations on their pain pattern. In jejunal diverticula the patient had epigastric pain radiating to the left side, first to the hypochondrium and, later, to the left lumbar and iliac regions. With ileal diverticula, on

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the other hand, he reported the pain as beginning lower down in the midline, even down in the hypogastrium, and radiating to the right lower quadrant. Martin and associates,[13] in 1954, reported that uncomplicated jejunal diverticula may produce a symptom complex consisting of postprandial abdominal discomfort, flatulence, and constipation, and they thought that, when this occurred, surgical treatment was usually indicated. Rankin and Martin,[17] in 1934, believed that no definite syndrome was associated with diverticulosis of the small intestine and, therefore, a clinical diagnosis could not be made. The primary complications are hemorrhage, obstruction due to enteroliths or adhesions, and diverticulitis with or without perforation.[1, 2, 7, 8, 9, 10, 11, 12, 14, 15, 16, 18, 19, 22, 23, 24]

Orr and Russell, in 1951[15] divided cases of jejunal diverticulosis into 3 groups: 1) diverticula not producing symptoms and found incidentally, 2) diverticula producing gaseous dyspepsia and mild abdominal discomfort, and 3) diverticula with complications requiring surgical procedures. No surgery was recommended for the first 2 groups.

In 1952, Charles W. Mayo and co-workers[14] recommended distending the diverticula with air as a means of identifying them at surgical exploration in patients who had unexplained hypochromic anemia.

MATERIAL

The purpose of this report is to present a case of jejunal diverticulosis with symptoms, roentgenologic findings, and gastroscopic findings suggestive of carcinoma of the stomach. Moreover, we want to emphasize that on certain occasions, jejunal diverticula produce symptoms which are relieved by excision of the involved intestine.

CASE REPORT

W. F., a Negro man 57 years of age, was first admitted to Illinois Research and Educational Hospitals Oct. 24, 1952. He claimed that, for the past year, he had been having dull, steady, upper abdominal pain occurring 2 to 3 hours after meals and lasting 1 to 2 hours. Occasionally the pain disappeared spontaneously, and, at other times, it was relieved by vomiting. The first episodes of pain were located in the left upper quadrant with radiation to the right, but recently it had been periumbilical in nature. The pain was most frequently brought on by rough foods. He had lost 25 pounds in weight in one year, although he had had no anorexia. Intermittently, during the past year, his abdomen had become tightly distended without relationship to meals.

Physical examination showed a thin, tall, Negro man who appeared chronically ill. The heart and lungs were normal. There was moderate distention of the abdomen most marked above the umbilicus. Peristaltic waves could be seen to originate just below the xyphoid and travel down and slightly to the right to an area just below the umbilicus. No definite mass could be palpated, but on, several occasions, palpation elicitated considerable tenderness just to the right of the umbilicus. Bowel sounds were hyperactive with many peristaltic rushes. There was no evidence of ascites.

Laboratory studies showed a normal urine analysis and a hemoglobin of 14 grams with a hematocrit of 45 per cent. The non-protein nitrogen was 33 mg. per cent. Cephalin flocculation tests were negative in 48 hours and the thymol turbidity was 5.8 units. The total proteins were 7.5 grams with a normal A/G ratio. Electrolyte determinations were normal. Stool examinations were positive for occult blood. Fasting gastric aspiration, 12 hours

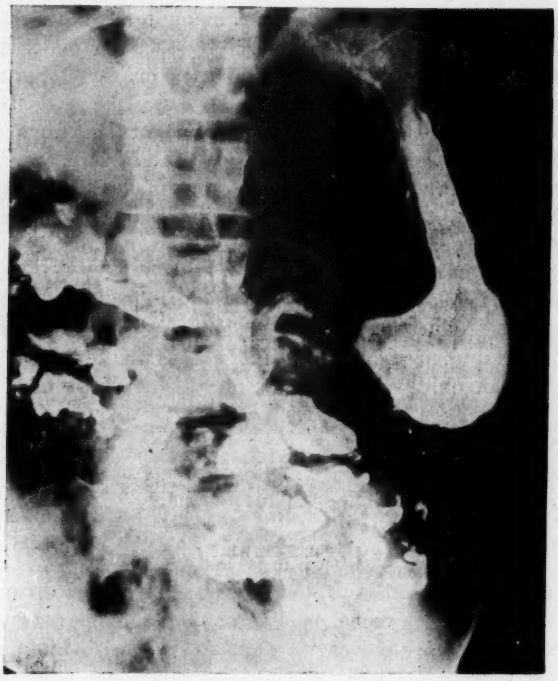

FIG. 1. Upper gastrointestinal roentgenograms showing an unusual accumulation of barium in the upper small intestine.

after 500 cc. of tea was given orally, was productive of 500 cc. with 7.5 units of free hydrochloric acid and 42.5 units of total acid. Serology was negative.

Chest roentgenograms were normal. A cholecystogram showed poor function with a question of stones in the gallbladder. An upper gastrointestinal series with barium showed a constant deformity of the greater curvature and proximal antral portion of the stomach. The mucosa in this region appeared to be involved in this process. Peristalsis did not pass through this portion of the stomach but recurred in the distal antral portion. There were several large diverticula in the duodenum. Progress roentgenograms showed an unusual conglomeration of barium in the upper small intestine suggesting a possible deficiency pattern (fig. 1).

Gastroscopy showed a superficial and hypertrophic gastritis. On the anterior wall and greater curvature of the fundus just distal to the cardia the mucosa was grayish in color and bulged into the lumen as though pushed by an intramural or extragastric mass adherent to the wall of the stomach.

On October 31, with a preoperative diagnosis of probable gastric carcinoma, the patient was explored through an oblique incision crossing the left rectus muscle high in the epigastrium. The stomach was found to be slightly thickened but no mass or other abnormalities were found. There were numerous large diverticula in the proximal jejunum extending over an area about 4 feet (1.2 m.) in length. The duodenal wall was greatly thickened and edematous indicating a moderate inflammatory reaction. There were likewise a few diverticula in the duodenum. Adhesions were present between the duodenum and the gallbladder but stones were not felt in the normal sized gallbladder. No other abnormalities were found

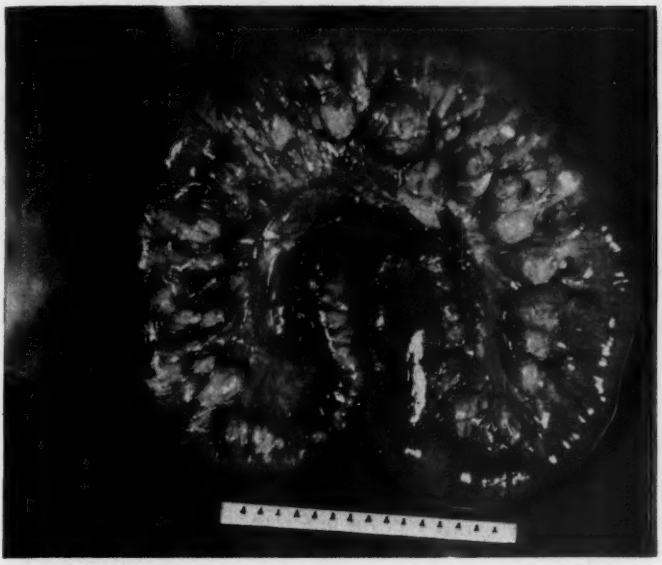

FIG. 2. The resected fresh specimen of jejunum containing multiple diverticula.

in the abdomen. It was decided to resect the involved portion of the jejunum. This was done and intestinal continuity was re-established by an end to end enteroenterostomy.

The resected fresh specimen (fig. 2) consisted of a 135 cm. length of jejunum and its attached mesentery. Along the mesenteric border were multiple large diverticula measuring up to 3 cm. in diameter. All of these were filled with fecal material. The lumen of the jejunum contained large quantities of soft, greenish-brown, mushy, foul-smelling material and much undigested food with carrots and potatoes readily identified. The diverticula were thin-walled and lined by mucosa. No ulcerated areas were found. The pathologic diagnosis was diverticulosis of the jejunum.

A repeat barium roentgenologic study of the upper gastrointestinal tract made on December 30, showed a normal appearing esophagus and stomach. There was evidence of at least 2 diverticula in the second portion of the duodenum and another one just distal to the ligament of Treitr. The stomach emptied slowly, but in 24 hours there was no evidence of retention of barium in the stomach or in any of the previously described diverticula.

On the patient's first return clinic visit Jan. 14, 1953, he was asymptomatic and had gained 10 pounds in weight. He was last seen March 16, 1955, at which time had gained an additional 13 pounds, was working full time, and was asymptomatic.

DISCUSSION

Jejunal diverticulosis has previously been established as a definite clinical entity, but, because of the paucity of cases reported, many factors including etiology, symptomatology, roentgenologic diagnosis, and therapy are still poorly understood.

Most case reports state that symptoms usually are absent or vague. The primary reported symptom is flatulent dyspepsia, and the principle reported sign is an unexplained presence of hypochromic anemia.

It has further been pointed out that very little dependence can be placed upon demonstration of jejunal diverticula by barium roentgenologic studies of the upper gastrointestinal tract. Weber,[25] in 1939, in the same article in which he claimed jejunal diverticula could be diagnosed most of the time by roentgenologic studies of the small bowel, described the findings in deficiency states as follows: "Fantastic agglomerations of the opaque suspension take place. In the normal small intestine the opaque suspension assumes a smooth, homogenous continuity; here part of it is collected in a pool in an isolated dilated segment, another part is clumped in an apparently unrelated amorphous mass, and the rest of it assumes the appearance of a flocculent precipitate throughout a long stretch of some other part of the small intestine". Even though this description closely resembles the findings in our case, in retrospect, it is believed that the large quantity of barium found in the upper small bowel, although not definitely outlining diverticula, should have made us suspicious of some pathologic process other than a deficiency pattern. Had we been more aware of the clinical entity of jejunal diverticulosis as one capable of producing such marked symptoms, this peculiar roentgenographic pattern might have made us suspect it preoperatively. Perhaps others who have operated upon patients who had jejunal diverticulosis which was not diagnosed preoperatively will find that upper gastro-intestinal barium roentgenologic studies showed a similar nonspecific pattern.

If jejunal diverticulosis is suspected or diagnosed, one is confronted with the problem of choosing between medical and surgical management. Although medical management was, it is true, not attempted for this patient because of the preoperative diagnosis of gastric carcinoma, it is believed that it would have been difficult, if at all possible, to alleviate his symptoms by this method. Patients presenting few or no symptoms, however, might well be best treated medically.

SUMMARY

A case of jejunal diverticulosis is reported in which the patient presented fairly severe abdominal pain, intermittent emesis and abdominal distention, and marked weight loss. Roentgenologic examination showed duodenal diverticula but none was seen in the jejunum which showed only an irregular pattern.

Symptoms disappeared completely following jejunal resection and the patient has remained asymptomatic up until the time he was last seen 30 months following resection.

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COMPLETE RECTAL PROLAPSE: THE ORR SUSPENSION TREATMENT

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The approach to surgical treatment of complete prolapse of the rectum which has been subjected to varying attitudes, now seems to be well established on sound functional anatomic principles. Most authors seem agreed that common basic factors in the development of complete prolapse of the rectum are an abnormally loosely attached rectum and redundant rectosigmoid with levator muscle separation. The presence of a deep cul-de-sac of Douglas is a uniform observation.

Moschovitz, as early as 1912[13], postulated that under the influence of intra-abdominal pressure a deep cul-de-sac formed the apex of a sliding hernia involving the anterior rectal wall. The sliding hernia thus developed is converted into a complete prolapse because of weakness of the transversalis pelvic fascia and separation of the levator ani muscles which permit penetration of the pelvic diaphragm. This concept guided surgical therapy in efforts to control the "*hernial sac*" by recreating a pelvic diaphragm. The role of a loosely attached and mobile rectum and rectosigmoid in permitting further propagation of the hernia is emphasized by Pemberton and Stalker as being the most important factor in its development.[15]

Thus it becomes evident that any procedure which fulfills the need for a safe standardized procedure with a smaller "*recurrence rate*" must be predicated upon the factors of genesis as categorized above. Consequently those steps essential for successful repair consist of strengthening the pelvic floor and controlling the abnormally loosely attached rectum and redundant rectosigmoid.

Contrariwise it becomes apparent that other procedures which do not control the factors of development would have limited usefulness and are of historic interest mostly.[3, 7, 8] These include, among others, such steps as reducing the calibre of the anus and lower rectum by cauterization of the rectal mucosa; Delorme's elliptical resections of the mucus membrane of the rectum with suturing wedge resection of the posterior rectal wall; Thiersch's silver wire ring around the sphincter; paraffin injections; Bier's reefing of the denuded outer cylinder of the prolapse; injection of pararectal tissue with sclerosing fluids; packing the posterior rectal space; and amputation or excision of the proximal segment.

Control of the pelvic floor defect usually has been approached perineally with suture of the levator ani muscles in the midline.[10, 6, 4] This approach continues to have wide application because of its low morbidity even with poor-risk patients. Even when combined with posterior resection of the redundant bowel, recurrence rates of 57 per cent[6] to 11 per cent[2] are noted with perineal pro-

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cedures. Therefore, additional steps are needed to control the abnormally loosely attached rectum and redundant rectosigmoid.

It is of interest to note that on April 21, 1908, Moschovitz, looking for the cul-de-sac to obliterate, used a posterior perineal approach with suture of the levators together and to the rectum. The patient died in four weeks from an ascending pyelonephritis. Moschovitz stated that "in spite of the correct anatomical principle involved," he abandoned the procedure in favor of the abdominal approach with obliteration of the cul-de-sac and rectopexy, reporting a cure rate of 55 per cent of 9 patients operated upon. Although he stated cul-de-sac obliteration and obliteration of the hernial sac were the means of successful repair, he still called attention to the importance of fixing the rectum to the coccyx and sacrum with laterally placed sutures. The importance of obliteration of the cul-de-sac was reiterated by Rankin and Priestly.[17] They reported the cases of 9 patients in whom a high pelvic diaphragm was recreated from above with satisfactory results in 7. Mayo[11] (1939) described a technic of fascial repair of complete prolapse by obliterating the cul-de-sac over a lattice of fascia at the superior inlet of the true pelvis, preventing recurrence of a deep pouch and perineal hernia in this manner. A similar approach using fascia to protect a thin pelvic diaphragm created by suturing the levators in the midline is recounted by Ripstein.[18] The fascia is fixed to the circumference of the true pelvic inlet.

The second consideration in successful repair of complete rectal prolapse is control of the abnormally loosely attached rectum and redundant rectosigmoid. Schroeder[19] (1908) described a repair of prolapse in which he sutured the levator muscles in the midline and emphasized as the important step pulling the levator ani muscles down and the intestine completely up before suturing the muscles first to the suspended rectum and then to each other. In 1913, Montgomery[12] described the findings in a 37 year old woman with a rectal prolapse. He found a long mesorectum, a deep retrouterine pouch, and a loosely attached rectum, sigmoid and colon. A suspension procedure was utilized for repair as follows: "The rectum was drawn up, and its peritoneal surfaces incised on either side as far back as could be done without endangering its blood supply, the peritoneum spread out and sutured on each side to the posterior parietal peritoneum, thus anchoring the rectum. The anterior surface of the rectum was sutured to the posterior surface of the cervix and the peritoneum on either side quilted together in such a way as to form a peritoneal floor and close the lower part of Douglas's pouch."

Ach[1] (1914) reported 2 cases of patients in whom strips of fascia lata 25 cm. long and 8 cm. wide were used to suspend the rectum retroperitoneally to the right ligament of Cooper and the right pubic bone, with no recurrence in two years and eight months.

The tendon of the right psoas minor muscle has been used to support the rectum tautly without recurrence one year later,[5] but since the psoas minor is so often absent, direct suture support of the rectum usually was entertained for suspension. It remained for Pemberton to emphasize that the rectum must be mobilized to be firmly fixed. Many early attempts at rectopexy were simple

sigmoidopexies not fixing the rectum at all. He calls attention to a cause for failure of intra-abdominal operations employing sigmoidopexy as omission of division of the pelvic peritoneum at its reflection along the lower sigmoid, thus preventing the rectum from being held taut. He reasoned that if the rectum were freed up posteriorly down to the coccyx and held taut and suspended away from the sacrum temporarily by a sigmoidopexy that a resultant ridge of presacral scarring would fix the rectum. A later follow-up and report of 44 cases with 4 recurrences (11.4 per cent) was presented.[16]

In 1947, Orr[14] described a method of suspending the rectum with fascial strips, and no recurrences were noted. In view of this apparent efficiency of the use of fascia lata to suspend the rectum, resection of the redundant sigmoid transperitoneally probably is not a vital step. This would eliminate an active cause of complications, and reduce the seriousness of the procedure. Posterior mobilization of the rectum as described by Pemberton, while not a part of the corrective procedure applied to the 2 patients presented here probably should be added to the technic to prevent recurrences if the cul-de-sac and rectum cannot be elevated tautly.

It is not the purpose of this presentation to attempt to standardize the Orr procedure nor to suggest that this is the procedure of choice to correct rectal prolapse to the exclusion or neglect of all others. For example, it would be difficult to improve morbidity rates and results any better than in the use of perineal rectosigmoidectomy and plastic reconstruction of the perineum as described by Altemeir and associates[2] for aged and debilitated patients. They noted only 1 recurrence in 9 patients.

The cases of 2 patients are here presented in whom a suspension operation as described by Orr was employed. No recurrence was encountered. In addition a follow-up of the 2 patients previously described by Levy and Johnson[9] operated upon, using a similar technic, are reported through courtesy of the authors. One of the patients now has a recurrence which the authors believe is due to the fact that the rectosigmoid was not held taut as the fascia lata was sutured in place.

In the patients of the cases presented the lower rectum was mobilized anteriorly and anterolaterally at the pelvic diaphragm, noting circular sphincter fibers around each as the lower level for fixing the fascia lata strips. If the rectosigmoid is held taut with gentle traction while the strips are fixed to the anterior spinal ligament at the sacral promontory, adequate suspension of the rectum to prevent a recurrence should be achieved.

TECHNIC

The technic used is a modification of the one described by Orr. Fascial strips about 1 cm. in width and 15 cm. in length were obtained through a single small thigh incision with a Masson stripper. A lower left paramedian incision is made from the pubis to above the umbilicus. The patient is placed in a Trendelenburg position and the abdominal contents are packed away from the pelvis with warm moist pads. A tape is passed through the mesentery beneath the lower sigmoid for traction (fig. 1). Gentle traction will hold the prolapsed rectosigmoid in normal

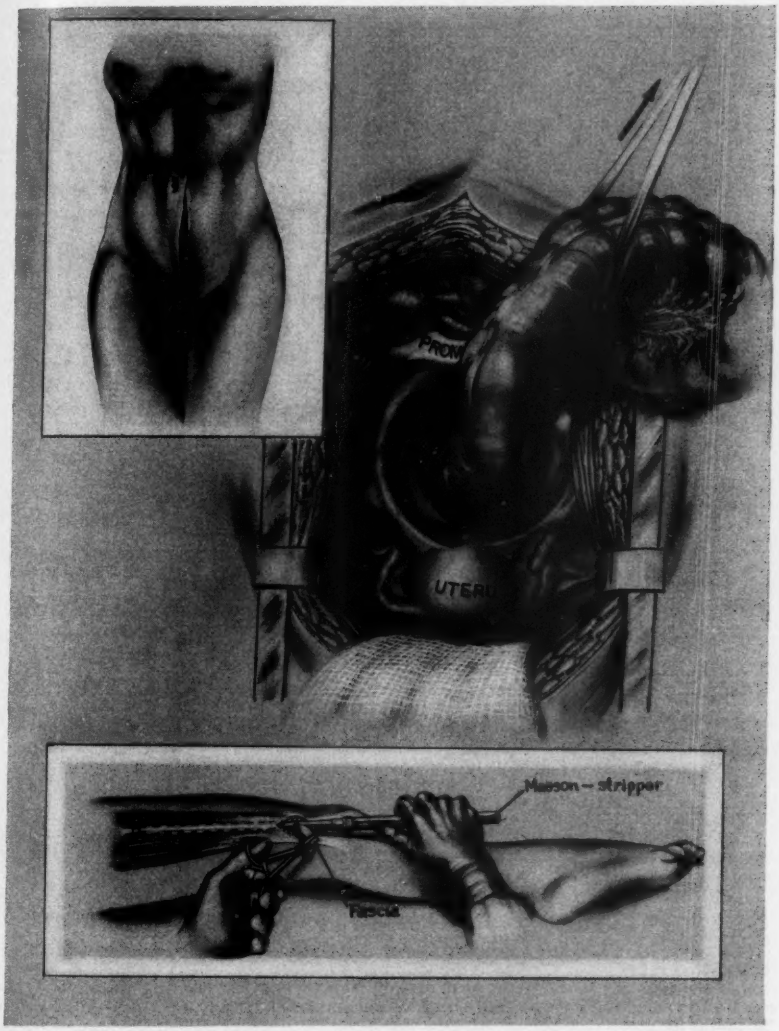

FIG. 1. (1) Upper inset shows type of abdominal incision used. (2) Sigmoid suspended with Tape showing deep cul-de-sac. (3) Lower inset shows use of Masson stripper to remove strips of fascia lata (Drawing by Joe Petro).

position. Just above the promontory of the sacrum the fascia is exposed through an inverted T shaped incision in the peritoneum. The rectum is mobilized anteriorly and anterolaterally. A strip of fascia is sutured to each side of the rectum for 7 to 8 cm. with a double row of interrupted sutures of fine cotton beginning deep in the sulcus at the internal sphincter fibers (fig. 2). The strip of fascia on

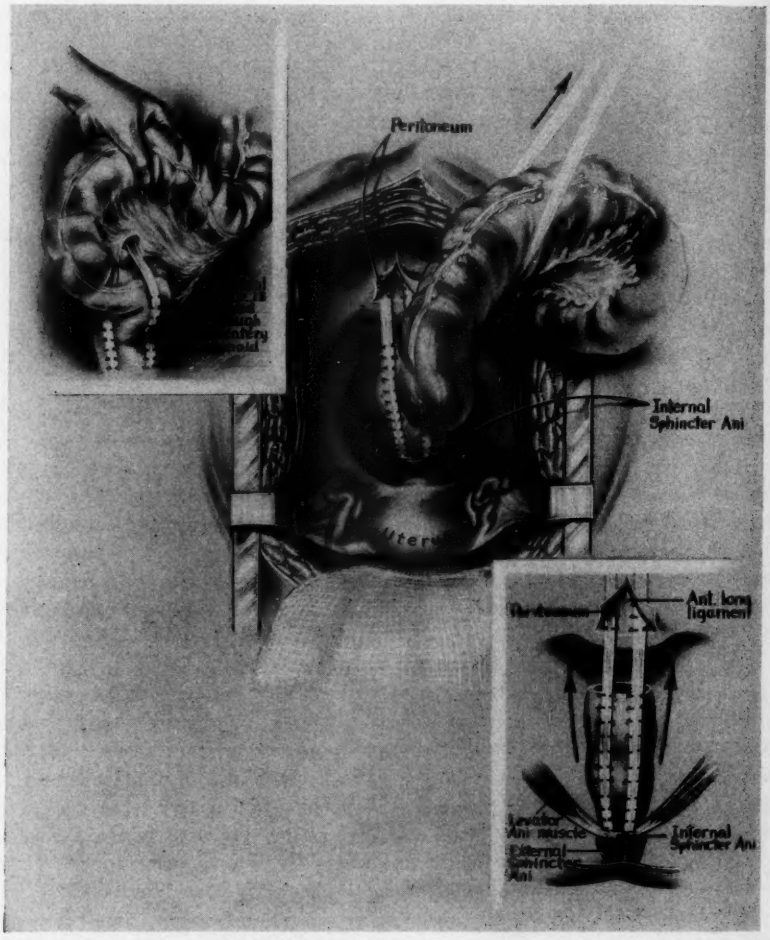

FIG. 2. (1) In upper inset the left fascial strip is passed through a puncture wound in the sigmoid mesentery. (2) Fascia of sacral promontory exposed through an inverted T-shaped incision in the overlying peritoneum. The rectum has been mobilized and fascial strips have been sutured to the internal sphincter muscle and to each side of the rectum. (3) Lower inset shows detail of suturing fascial strips to internal sphincter muscle and rectum (Drawing by Joe Petro).

the left is passed through a puncture wound made in the mesentery of the recto-sigmoid. While the rectum is held suspended a firm sense of immobility is noted. Traction on the rectum is maintained while the upper ends of the fascial strips are sutured to the anterior spinal ligament above the promontory of the sacrum. Interrupted cotton sutures are used to attach both margins of the fascial strips to the ligament, a distance of at least 2 cm.

The cul-de-sac is completely obliterated by two or more rows of interrupted

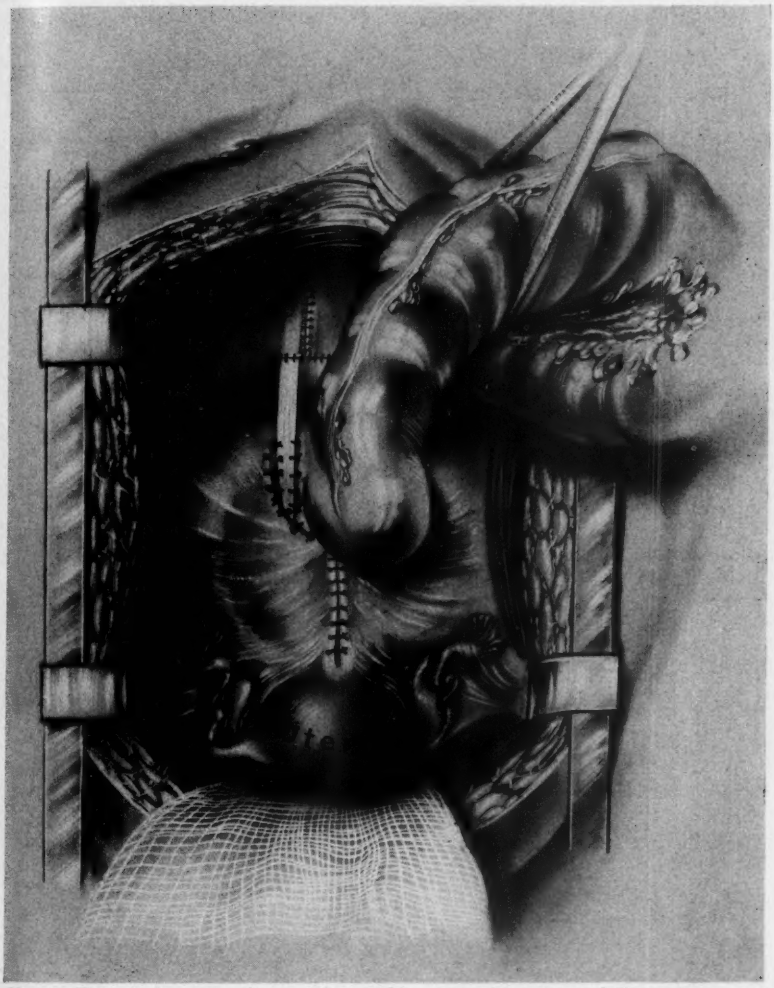

FIG. 3. The cul-de-sac has been obliterated by rows of sutures and the peritoneum has been sutured in the midline to the rectum to cover the fascial strips (Drawing by Joe Petro).

cotton sutures placed across the pelvis. The peritoneum is sutured to the anterior wall of the rectum as each row of sutures is placed.

The pelvic operation is completed by suturing a fold of peritoneum to the rectum on each side to cover the fascial strips (fig. 3).

The abdominal and thigh wounds are closed with cotton.

CASE REPORTS

Case 1. A 26 year old white mine worker who had an easily reducible rectal prolapse for many years was admitted to St. Joseph Hospital on April 14, 1952. The rectal prolapse had

become worse for three years and was aggravated by the squatting position assumed in his work.

Proctoscopic examination was negative a distance of 24 cm. The anus was hypotonic and patulous. A colon roentgenogram made on April 15 showed a marked redundancy of the sigmoid and of the hepatic flexure.

Operation was done on April 19, 1952. The cul-de-sac was deep and level with the coccyx; the bladder was greatly enlarged. Because of the narrow caliber of the deep cul-de-sac, it was impossible to suture the levator ani muscles in the midline.

The rectum was suspended and fixed with fascial strips as described. The pelvic floor was then elevated to the level of the opening of the true pelvis by obliteration of the cul-de-sac with multiple cotton sutures. No antibiotics were used. The following day there was a urinary retention of 750 cc. The bladder was decompressed by continuous drainage with a Foley catheter. On April 22, he was walking, passed rectal flatus, and was started on water and fat-free broth by mouth. On April 24, a nonresidue diet was instituted. The bladder catheter was removed. A regular diet was resumed on April 26. On this date the abdominal wall sutures were removed. The first bowel movement occurred following a plain water enema. He was discharged from the hospital on April 30, 1952. The patient has remained well without complaints and without recurrence for nearly three years.

Case 2. A 38 year old white housewife with 5 children, ages 21 to 13 years, was admitted to St. Joseph Hospital on July 13, 1953. Eighteen years before she noted a small rectal prolapse. For the past 10 years this prolapse has protruded 5 to 8 in. and in the past year has increased in size and extension. Only a slight protrusion is noted on walking, but a sneeze, strain or bending over would *"bring it out"* to its full extent. Nausea was noted when the prolapse was at its largest size. The prolapse would cut off the urinary stream and prevent micturition until reduced. Proctoscopy previously was negative up to 23 cm.

At operation (July 14, 1953) it was found that the uterosacral ligaments were widely separated forming an anterior rim for the deep cul-de-sac. The pelvis itself and the cul-de-sac extended 3 to 4 cm. beyond the tip of the coccyx. The suspension operation as described was done and the cul-de-sac was obliterated with multiple small cotton sutures. The uterosacral ligaments were sutured to each other in the midline and the round ligaments were sutured to the posterior fundus, stabilizing the uterus.

On July 16, she began to tolerate water and fat-free broth, and a regular diet was begun July 17. Following a normal bowel movement, she was discharged July 18. Recovery was uneventful and complete, with no recurrence to date (March 1955). It was interesting to note that a patulous anus, which easily admitted four fingers preoperatively, recovered its tone almost completely on the fourth postoperative day.

DISCUSSION

Through the courtesy of Levy and Johnson a follow-up of their previously reported cases is presented. The following excerpts from their letter are quoted. "Mr. H. E. K. (Case 1 in our report) is now 64 years old. He has had an excellent result from the operation which was performed six years and four months ago. There has been no recurrence of the prolapse at any time, and there is no protrusion even with heavy straining. In addition, the marked fecal incontinence of which the patient complained before operation is now *'about 75 per cent improved'*. He spills a small amount of liquid feces on occasion, but is able to keep from soiling himself by wearing a small pad".

"Mr. F. C. (Case 2) is now 32 years old. The prolapse was repaired six years ago. There was no recurrence for a period of three years following operation. Then the patient noticed that with very heavy straining about 2 to 2.5 cm. of rectum could be extruded through the anus. This is compared with 7 to 8 cm. of prolapse

before operation. The condition has remained static during the period of three years. At the present time moderate straining, such as is required for a bowel movement, will not produce a prolapse. He has normal evacuation without urine difficulty".

"As far as one can judge from these 2 cases, I believe that the operation is sound. Although the second case must be considered a failure, the patient remained much improved over his preoperative condition. The moderate recurrence might be attributed in part to the fact that he is a lean '*ptotic*' individual. Perhaps more important is the fact that the rectum was not held completely taut when the fascial strips were being sutured to it, so that the lowermost edges of these strips did not quite reach to the bottom of the cul-de-sac when the rectum was pulled taut."

SUMMARY

The literature on surgical treatment of complete rectal prolapse is reviewed to point out the factors in the development, namely, a deep cul-de-sac of Douglas, levator muscle separation, and an abnormally loosely attached rectum and mobile rectosigmoid.

A procedure predicated upon these factors of genesis for repair of complete rectal prolapse is described. This is a reaffirmation of the concepts proposed by Orr. Two new patients who were successfully treated by this technic are presented and follow-ups on 2 previously reported cases are given.

Suspension of the rectum with fascia lata apparently provides fixation of the rectum and rectosigmoid to the point that resection probably is no longer necessary.

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HISTORICAL

ANCIENT ANODYNES: A HISTORY OF ANESTHESIA PRIOR TO 1750*

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For ages man has suffered pain and has sought relief from pain. From nearly all the ancient civilizations which have left written records have come descriptions of methods or substances used to allay suffering and to produce sleep. In this paper some of the means by which the ancients endeavored to find relief from pain will be related.

The book of Genesis, believed to have been written about 4000 B.C., contains the first written description of the relief of surgical pain. "And the Lord God caused a deep sleep to fall on Adam, and he slept: and he took one of his ribs, and closed up the flesh instead thereof."[11]

A Babylonian clay tablet inscribed about 2250 B.C. reveals a remedy for the pain of dental caries. Printz stated that a "cement consisting of henbane seeds in a powdered form was mixed with gum mastic and applied to the cavity."[27]

Evidence of the knowledge of pain-relieving drugs is found in ancient Egypt. In the Ebers Papyrus, written about 1500 B.C., mention is made of the frequent use of opium, hellebore and hyoscyamus. There is abundant evidence that the Papyrus was copied from various sources, some many centuries old.[26]

It is probable that primitive man employed digital compression of the carotid arteries to produce loss of consciousness. Anesthesia by this method is said to have been practiced by the ancient Assyrians before performing the operation of circumcision. The word carotid is literally translated from the Greek and Russian to mean sleep and the carotid artery "the artery of sleep". Pressure on the jugular veins of the neck was also said to produce insensibility. Aristotle said of the jugular veins; "if these veins are pressed externally, men, though not actually choked, become insensible, shut their eyes and fall flat on the ground."[28]

In Greece the God of Medicine, Aesculapius, was supposed to have used a potion called "nepenthe" to produce insensibility for his surgical patients.[17] Nepenthe (from the Greek "ne", negation, and "penthos", sorrow or pain) was referred to by Homer (1149 B.C.) in the *Odyssey*, Book 4: "Then Helen, born of Zeus, planned otherwise. Straightway into the wine of which they were drinking she cast a drug to assuage suffering and to cause forgetfulness of all ills. Whosoever should drink this down, when mingled in the bowl would not, in the course of that day, let a tear fall down over his cheeks, not even if before his face his brother or his beloved son they should slay with the sword, and with his own eyes he should behold it. Such cunning drugs had the daughter of Zeus, potent

* Written when a senior student as one of the requirements for graduation at The University of Kansas School of Medicine, Kansas City, Kansas.

drugs, which Polydamna, the wife of Thor, had given her; a woman of Egypt, for there the ploughed earth, giver of food, bears the greatest store of drugs, many that are potent when mixed and many that are baneful."[13] Homer referred in his *Iliad* to a root which had pain-relieving powers. The passage in which Patroclus treated Eurypylus is as follows:

> "Cut out the listing shaft; and from the wound
> With tepid water cleansed the clotted blood;
> Then pounded in his hands, the root applied.
> Astringent, anodyne, which all his pain
> Allay'd; the wound was dried and staunched the blood."[12]

Robinson said, "Some authors have contended that nepenthe was no actual drug but that Homer was referring to the charm of Helen's conversation."[28] Hume[15] quoted Oswald Schmiedeberg who in 1918 summed up the work of earlier investigators and came to the conclusion that opium was the only drug which satisfied the description of the drug used by Helen of Troy in the *Odyssey*. He further stated that reference to the poppy was made by Hippocrates in his writings so there is no reason to believe that the poppy was unknown to the ancient Greeks. Reference in the *Iliad* to a root which had the properties of an anodyne leads me to believe that mandragora was known to the Greeks of that time.

In India the great Hindu physicians Charaka and Susruta are credited with mentioning anesthetic procedures. Susruta wrote, "Wine should be used before the operation to produce insensibility to pain."[20] For the same purpose Indian hemp (cannabis indica) was used by inhalation of fumes. Major[21] also credits Susruta as being a pioneer in anesthesia and states that the physician made use of henbane (hyoscyamus niger) as well as Indian hemp to produce insensibility to pain. Indian hemp was known also by the name "hashish" and the plant was endowed with such epithets as "leaf of delusion, exciter of desire, increaser of pleasure, cementer of friendship, the laughter-mover, and causer of the reeling gait."[28] The stage of sleep and insensibility to pain was preceded by a stage of excitement. This is well described by the ancient Greek historian Herodotus[10] of the fifth century B.C. who stated concerning the baths of the Scythians: "The Scythians then take the seed of this hemp, and creeping under the rugs, they throw it on the red hot stones; being so thrown, it smoulders and sends forth so much steam that no Greek vapor-bath could surpass it. The Scythians howl for joy in the vapor-bath."

In China about 255 B.C., according to the *Chinese Annals of History*,[15] there lived a very famous and successful physician called Pien Ch'iao. No name stands higher in the annals of Chinese medicine and the honor paid to him is wholly comparable to that which the western world pays to the memory of Hippocrates. An account of one of his successful operations, as related by the historian Lieh Tze, follows: "Two men, Lu Kung-Ha and Chao Ch'i-Ying, fell ill and came together to seek treatment from Pien Ch'iao. After treating them, when both were recovered he said, calling them by name, 'The illness from which you suffered previously came to your organs from external influences and was susceptible to medical treatment. You now have a malady which attacked both of you together.

Do you wish it treated?' Both men asked that he first give them the results of his examination. Pien Ch'iao addressed Kung-Hu and said, 'Your will is strong but your spirit is weak; hence you are strong in one respect and weak in another. The will of Ch'i-Ying is weak, but his spirit is strong. If your hearts were exchanged there would be an equilibrium and the result would be good.' So then Pien Ch'iao caused the two men to drink a drugged wine, which made them insensible, as if dead, for three days. He cut open their chests, investigated and exchanged their hearts and replaced them, employing potent drugs. When they recovered consciousness both men were as at the first, took their leave and went home." Pien Ch'iao purportedly used a "toxic wine". Since opium was not known in China at this time, being introduced by the Arabs in the ninth century A.D., Hume believed that the narcotic used may have been from the seeds of the female hemp plant (cannabis sativa). The Chinese called it "ma".

Another famous Chinese physician was Hua T'o, born about 190 A.D. He used an anesthetic effervescent powder which was placed in wine. When taken orally by his patients it would intoxicate them and make them completely insensible to pain while he performed his surgery the descriptions of which are "legend".[15] The preparation used was called "mario" and is believed to be derived from Indian hemp.[8]

From 54 to 68 A.D. lived Pedanius Dioscorides, a famous Greek army surgeon in the service of Nero.[16] He composed a Materia Medica which described the use of mixtures of hyoscyamus, opium and mandragora as agents to produce surgical anesthesia. A potion was prepared in wine to be taken orally as a soporific draught or to be given per rectum by suppository.[21] Dioscorides, in addition to having been among the first to mention the use of surgical anesthesia and the first to mention the use of rectal anesthesia, also mentioned a form of local anesthesia which he used.[14] It involved the use of the "Stone of Memphis", and he remarked in describing the effects of this stone, "It is said that this (stone) being beaten small and smeared upon the places to be cut or cauterized it produces anesthesia without danger."[21] The stone was treated with vinegar before its use. According to Kleiman[18] it is possible that the anesthetic effect obtained was due to the numbing effect of carbon dioxide, as the "Stone of Memphis" was composed of carbonates which in coming in contact with the acetic acid in the vinegar is said to produce carbon dioxide.

It is noteworthy that Dioscorides employed the term "anesthesia". Mörsch and Major[23] stated that he was the first person known to use the word as meaning an absence of sensation caused by drugs. Plato (400 B.C.) is credited with using the word to express the absence of feelings or e.g. "for the condition where the impulse is not transmitted to or announced to the brain." Robinson[28] quoted Plato in the *Timaeus* in discussing why God placed dense flesh over certain bones and little flesh over other bones: "At the junctions of the bones, except where reason revealed some necessity for its existence, He made but little flesh to grow, lest by hindering the flexions it should make the bodies unwieldy, become stiff in movement or else through its size and density, when thickly massed together, it should produce 'anesthesia', owing to the rigidity. . . ."

In the days of the Roman Empire soporifics and anodynes were known. Pliny

in 79 A.D. wrote one of the first descriptions of the mandragora wine: "It has a soporific power on the faculties of those who drink it. The ordinary potion is half a cup. It is drunk against serpents and before cuttings and puncturings, lest they should be felt."[16] The plant "helenium" is described by Pliny and it harks back to the Homeric nepenthes. "The helenium is said to have had its origin in the tears of Helen, and hence it is that the kind grown in the island of Helena is so highly esteemed." Pliny says that taken in wine the helenium is believed to have "a similar effect to nepenthes which has been so much vaunted by Homer as producing forgetfulness of all sorrow."[28]

Celsus, who lived in the first century A.D., in his De re Medica wrote, "Pills are numerous and are made for various purposes. Those which relieve pain through sleep are called anodynes; unless there is an overwhelming necessity it is improper to use them; for they are composed of medicaments which are very active and alien to the stomach. There is one, however, which actually promotes digestion, it is composed of poppy-tears and galbanum (four grams each), myrrh, castory, and pepper (eight grams each). . . . Another, worse for the stomach but more soporific consists of mandragora (one gram), celery seed and hyoscyamus seed (sixteen grams each) which are rubbed up after soaking in wine." Celsus wrote further of soporifics: "Beneficial for. . . composing the mind itself is saffron ointment with orris applied to the head. If in spite of this patients are wakeful, some endeavor to induce sleep by draughts of a decoction of poppy or hyoscyamus; others put mandrake apples under the pillow; others smear the forehead with cardamonium balsam or sycamine tears."[28] The sycamine tears are from the mulberry tree. These authors also mentioned the use of lettuce as a soporific. Galen shunned the strong narcotic drugs but enthusiastically recommended lettuce for its calming effect.[28] Usually the milky juice of the stem, "lactucarium", was used. It was active only if collected when the plant was mature.[29] Later during the Renaissance the seeds were preferred to the juice and Platearius of Salerno wrote an interesting sedative prescription: "For producing sleep, the seeds of lettuce are made up with human milk and egg white into a plaster, which is placed about the temples; or the seeds given in milk and this will cause sleep."[29]

One of the most frequently mentioned anodynes of the ancients was hyoscyamus or "henbane". "The name hyoscyamus (swine-bean) indicates that it was thought good for hogs, while henbane plainly indicates that it was considered poison for fowls."[28] According to Dioscorides hyoscyamus was used to catch birds. A quantity of it was burned beneath the tree where the birds nested. Many of the birds who inhaled the fumes fell to the ground senseless and he relates although some perished others could be revived by dropping vinegar in their nostrils.[29] He called attention to its pain relieving qualities; "First of all the juice and that which is made of the dry seed is prepared for lotions to take away pain and for the sharp and hot rhume and for ear pains and grief about the matrix."[28] Dioscorides was aware of the drug's toxicity and wrote, "If it is drunk or eaten it causes that kind of insanity or turbulent counterfeit of sleep which the layman calls 'milimundrum' for it produces alienation of the mind."[30] Three kinds of hyoscyamus were recognized, the white, the red, and the black. The

black however was said to be too poisonous for human use. The seeds of the plant were used by preference and they were to be collected only during the "dog days". Hyoscyamus was generally combined with opium and although empirical, the combination was, of course, less toxic than either drug used alone, albeit no one seems to have noticed this.[29]

Other herbs recognized by the ancient Greeks as possessing sedative powers were black hellebore, dittany, hemlock and hops. Hippocrates, fifth century B.C., mentioned the use of black hellebore or "hellebore niger" as a purgative. A century later Theophrastus[31] noted the sedative properties of the drug and stated, "The properties of some plants are hurtful, they take hold it is said like fire and burn; for hellebore too soon makes the head heavy, and men cannot go on digging it up for long; wherefore they first eat garlic and take a draught of neat wine therewith."

Dittany is another herb which found its way into Greek literature. It was grown on the Isle of Crete. Aristotle tells that the wild goats of Crete when wounded by arrows were said to seek out dittany which was supposed to have the property of ejecting arrows from the body without pain. Virgil[33] in the *Aeneid* tells of when Aeneas was wounded and Venus administered dittany: "Hereupon, Venus, smitten by her son's cruel pain, with a mother's care plucks from Cretan Ida a dittany stalk clothed with downy leaves and purple flower; not unknown is that herb to wild goats, when singed arrows have lodged in their flank. This Venus bore down, her face veiled in dim mist; this she steeps with secret healing in the river water poured into bright-brimming ewer, and sprinkles ambrosia's healthful juices and fragrant panacea." Virgil then related the result of the celestial anesthetic, "With that water aged Iapyx laved the wound, unwitting, and suddenly, of a truth, all pain fled from the body, all blood was staunched deep in the wound. And now following his hand, without constraint, the arrow fell out and new-born strength returned as of yore."

Hemlock, famous as the death potion of Socrates was another ancient anodyne. The Greeks discovered little use for this drug, other than a quite satisfactory State poison, as the poison in its leaves was not constant. Its pain relieving power varied according to the weather and climate, the conditions under which it was grown and the age at which it was collected. Bright shining leaves often yielded a very weak narcotic. The narcotic was said to be the strongest when the flowers of the plant began to fade.[28]

In the warehouses which were used to store hops for the brewing of beer it was noted that workers had a tendency to become very drowsy. Thus it became known that the hop plant (humulus lupulus) had narcotic properties. Later the hop pillow became a popular sedative for restlessness and insomnia.[28]

Probably chief among the anodynes of the ancients was mandragora or mandrake. As the name mandrake implies, much mystery and magic was connected with powers of this drug. Many tales grew up concerning the proper procedures for its collection, use, and disposal. Mörsch and Major[23] relate some of the superstition and mystic rites concerned with the plant: "The most potent plants were supposed to grow on the gallow hills, and they were harvested at new moon. If one

simply pulled up the plant he would either die or go mad. To protect against the diabolic spirits of the plant, one had to face west and cut three rings around oneself in the air with a sword. Cautiously, then, the earth around the root had to be loosened and removed so that not even the finest root hair was damaged. When only one hair remained the mandragora was tied to the tail of a black dog, who did not have a single white hair, or to the left leg of a black cock. When wrenched from the earth the plant would shriek so discordantly that any ear witness would die. With a horn one must outblast the clamor of the mandrake ears wax deafened. The poor animal who was forced to do this dreadful task of pulling up the plant would tumble stone dead.

The mandragora could turn his owner into a genius or a demon, it could protect him against wounds and death in battles, it could endow him with all the wealth and beautiful women he might desire and give him unlimited potency. It was mandatory to get rid of it before death or go straight to hell. No one could destroy the mandragora. It could neither be crushed, burned nor thrown away. It had to be sold, but only for a price lower than that paid for it."

Many authors tell of the soporific and analgesic properties of the mandrake. As early as 230 B.C. Theophrastus in his *History of Plants* wrote of the medicinal properties of mandragora. He stated, "The leaf mixed with meal is useful for wounds and the root for erysipelas. When scraped and steeped in vinegar it is also used for gout, for sleeplessness and for love potions. It is administered in wine or vinegar. . . ."[32] Dioscorides (vide supra) made extensive use of mandragora wine as well as its use as a constituent in rectal suppositories used for anesthesia. As will be related later mandragora was a principal ingredient in the soporific potions and soporific sponges used for anesthesia during the Middle Ages and Renaissance. In proof of the anesthetic properties of mandragora in 1888 Benjamin Ward Richardson procured specimens of the root from Greece and followed the exact technic described by the ancients in obtaining a vinous tincture.[14] He macerated the root in alcohol diluted with five times its weight of water, for four weeks. His experiments, using the wine produced, proved that animals could be very well anesthetized and the wine was of a very potent quality. Richardson concluded that the drug's action depended on the presence of an alkaloid not unlike if not identical with atropine. He noted that if an overdosage was given respiratory arrest occurred before cardiac arrest and he proposed that the drug perhaps might be once more employed to deaden the pain of a surgical operation.[32] Richardson found the active principle of the drug was more soluble in water than in alcohol and surmised the alcoholic content of the ancient mixtures was added for its preservative as well as its intoxicating properties. The effects produced after oral or subcutaneous administration of the tincture were recorded as: "narcotism, dilatation of the pupil, paralysis of motion and sensation, excitement during recovery if the dose was not fatal, and sleep and paralysis if the dose were too potent."[32] Richardson also called attention to the powerful local anesthetic effect of the drug. "On applying the tincture to my lips there was produced an insensibility which lasted for more than an hour and was very decided."[32] In about 1900 the active alkaloids from the root were extracted

FIG. 1. Medieval illustrations of the plant Mandragora

and identified as hyoscyamine, scopolamine, norhyoscyamine and another alkaloid called "mandragorine".[32] Aside from its narcotic properties mandragora was purported to have the power of removing sterility and to stimulate the passion of love.[32] According to Thompson dried mandrake roots, especially those shaped like a woman holding a child in her arms, are still highly prized by women in Syria and Turkey, and carried as a charm to promote fecundity.[32] The root is usually bifid and many pictures of the root bearing resemblance of a human being are found throughout the ages (fig. 1). The plant early was referred to as being sexual, the male usage being first to be employed. Later the plant came to be regarded as bi-sexual and descriptions of mandrake, male and female were recorded and later even the female species was called "womandrake". Keys[17] stated the drug was employed for centuries by the Chinese and Hebrews in cases of criminologic investigation. The accused were forced to drink a concoction in the form of an infusion with other drugs. This produced a confused mental state which often led to a confession of the crime. The mandragora also was administered to help alleviate the sufferings and tortures inflicted on the accused prisoners. "In such an event it was known as the potion of the condemned."

Other drugs have been mentioned in the writings of the peoples of the Near East. From the writings of the Hebrew *Talmud* a narcotic called "samne de shinta" was mentioned.[6] The *Talmud* was written during Jewish captivity in Babylon prior to 500 A.D. The drug was supposed to have been used "to deaden the pain present and occasioned by the operation."[20] The *Arabian Nights* contains some references to soporific drugs, e.g. henbane: "Presently he filled a cresset with firewood on which he stewed powdered henbane and lighting it went round about the tent with it till the smoke entered the nostrils of the guards and they all fell asleep, drowned by the drug."[28] The drug was called "bhang" by the Arabs. Major[21] mentioned the Arab, Jesu Haly, a Christian physician and ophthalmologist who practiced in Bagdad in the late eighth century. In his book of

ophthalmology he spoke of anesthesia in four places. In his description of the operation for removal of hydatids from the eyelids, he remarked; "In case the patient is one of those who can't hold still and cause trouble, put him to sleep and let one assistant hold his head and the other his arm." Major stated Haly elsewhere described mandragora and opium as drugs which produce sleep so it is highly probable that these were the anesthetics employed. Another famous Arabian physician was Ibn Sina, better known as Avicenna. He collected and codified all the then available medical knowledge in his *Canon of Medicine*. Later translated into Latin it became the authoritative medical textbook of Europe for six centuries. Avicenna recommended opium, henbane and mandrake as narcotics. He said, "If it is desirable to get a person unconscious quickly without his being harmed add sweet smelling moss or aloeswood to the wine. If it is desirable to procure a deeply unconscious state, so as to enable the pain to be borne, which is involved in painful applications to a member, place darnel-water into the wine or administer fumitory, opium, hyoscyamus (half dram dose of each), nutmeg, crude aloes-wood (four grams of each). Add this to the wine; and take as much as is necessary for the purpose. Or boil black hyoscyamus in water with mandragora bark until it becomes red and then add this to the wine."[3] An account of anesthesia by inhalation on the Hindu king Bhoja who lived about 927 A.D. is made by Leonardo.[20] The fumes of the drug "sammohine" were used to put him to sleep for a trephination for a brain tumor.

Most of the other reports on anesthetic and analgesic preparations come from Europe. Ashley Montagu[22] referred to a fourth century A.D. account of the anesthetic effects of certain drugs. He quotes St. Hilary of Poitiers, (300–367 A.D.), a churchman of that time: "The nature of our bodies is such, that when endued with life and feeling by conjunction with a sentient soul, they become something more than inert, insensate matter. They feel when touched, suffer when pricked, shiver with cold, feel pleasure in warmth, waste with hunger and grow fat with food. By certain transfusion of the soul, which supports and penetrates them, they feel pleasure or pain according to the surrounding circumstances. Where the body is pricked or pierced, it is the soul which pervades it that is conscious and suffers pain. For instance a flesh wound is felt even to the bone, while the fingers feel nothing when we cut the nails which protrude from the flesh. And if through some disease a limb becomes withered it loses the feeling of living flesh: it can be cut or burnt, it feels no pain whatever because the soul is no longer mingled with it. Also when through some grave necessity part of the body must be cut away, the soul can be lulled to sleep with drugs, which overcome the pain and produce in the mind a death like forgetfulness of its power of sense. Then limbs can be cut off without pain; the flesh is dead to all feeling and does not heed the deep thrust of the knife, because the soul within it is asleep."

Apuleius, a fifth century compiler of Greek botanico-medical material tells of mandragora: "If anyone eat it he will die immediately unless he be treated with butter and honey and vomits quickly. Further if any one is to have a limb mutilated, burnt or sown, he may drink half an ounce with wine, and whilst he sleeps the member may be cut off without any pain or sense."[25]

Henry Sigerist found in the Bamberg *Antidotarium*, which was written about the ninth century A.D., a recipe perhaps the first in Europe for a "soporific sponge". About the same time at the famous French monastery of Monte Cassino another recipe for preparing a soporific sponge was used:[21] "Hypnotic Aid, that is a soporific suitable for those who are treated by surgery, so that asleep, they do not feel the pain of cutting. Rx; opium (one half ounce), mandragora the juice from the leaves (eight ounces), the juice of fresh hemlock, hyoscyamus (three ounces of juice) together with sufficient water so that it forms a liquor, and then absorb in a fresh dry sponge and dry it carefully. And when thou woulds't employ this sponge, dip it in warm water, and place it over the nose and cause the patient to breathe deeply until he sleeps. And when thou woulds't wake him up apply to his nose another sponge well soaked in vinegar and thou wilst end the sleep." Further mention of this formula for preparation of a soporific sponge was made in Nicolas of Salerno's famous *Antidotarium*[24]. This was a textbook of the medical school and was composed of various prescriptions in common use at the time. These were discussed by masters of the school, revised and corrected.[21] The formula is as follows: Spongia Somnifera: "Take . . . of opium thebaicum, juice of hyoscyamine, unripened berry of black berry, lettuce seed, juice of hemlock, poppy, mandragora, ivy . . . . Put all these together in a vessel and plunge therein a new sea-sponge just as it comes from the sea, taking care that fresh water does not touch it. And put this in the sun during the dog-days until all the liquid is consumed. And when there is need dip it a little in water not too warm and apply it to the nostrils of the patient and he will quickly go to sleep. When moreover you want to awaken him, apply juice from the root of fennel and he will soon bestir himself." Another Salernitan who described a soporific sponge in his *Compendium* was Gilbertus Anglicus (about 1180–1250). His "confectis soporifera" consisted "of opium hyoscyamus, poppy, mandragora, ivy, blackberries, lettuce and dodder." He rouses the patient with vinegar also. Major states he also described a soporific drink containing poppy, opium, and lettuce.

In Italy, about 1200 A.D., Hugh of Lucca and his son Theodoric used a soporific sponge in their surgery which Theodoric described.[30] The formula is identical with the Salernitan whence he probably obtained it.[21] Gossen[9] states the sponges were "moistened and tied in front of the nose and mouth of the patient to be operated so that the juices could exert their action by dripping into the gastro-intestinal canal." This seems logical as most of the ingredients were nonvolatile and it would be difficult to see how much anesthesia could be so obtained by inhalation. Mention is made however by Fulop-Miller[8] that mandragora pillows were used for anesthesia and he states, "No less a man than St. Benedict, we are told, being about to amputate a leg of Emperor Henry II, put the patient to sleep upon a mandragora pillow so that the operation could be performed without causing any pain."

That soporifics administered prior to surgery were an accepted thing in the Middle Ages is borne out in their mention by the poets and writers of the time. Thus from Boccaccio's *Decameron*[4] in the fourth day, and tenth story as told by

Dioneo there is an illustration of anesthesia: ". . . It happened that there came to the attention of the physician (Maestro Mazzeo della Montagna) a patient with a gangrenous leg and when the master had made an examination, he told the relatives that unless a decayed bone in the leg were removed either the entire leg would have to be amputated or the patient would die; moreover, if the bone were removed, the patient might recover, but he refused to undertake the case except as if the man were already dead. To this the relatives agreed and surrendered the patient to him. The doctor was of the opinion that without an opiate the man could not endure the pain and would not permit the operation and since the affair was set for evening, he distilled that morning a type of water after his own composition which had the faculty of bringing to the person who drank it sleep for as long a time as was deemed necessary to complete the operation."

Magister Salernus *Compendium*, written about 1170 A.D., mentions the use of a mixture of opium, hyoscyamus and mandragora as a local anesthetic.[21] William of Saliceto (1200—1278), an Italian, was said to have devised a number of plasters and ointments containing opium and hyoscyamus which he used for anesthesia. He advised against leaving them on for too long a time as it would retard healing.[21]

Guy de Chauliac, a French surgeon who wrote *Great Surgery*, a text used for centuries by surgeons, continued to use the sponge similar to that described by Theodoric. John Arderne of Newark-on-the-Trent gave a different formula which he used for producing anesthesia:[28] "An ointment with which if any man be anointed he shall suffer cutting in any part of his body without feeling or aching. Take the juice of henbane, mandragora, hemlock, lettuce, black and white poppy, and the seeds from all these aforesaid herbs, if they be had, in equal quantities, of Thebian poppies and of poppy meconium one or two drams with sufficient lard. Braise them all together and thoroughly mix in a mortar and afterward boil them well and let them cool. And if the ointment be not thick enough add a little white wax and then preserve it for use. And when you wish to use it anoint the forehead, the pulses, the temples, the armpits, the palms of the hands and the soles of the feet and immediately the patient will sleep so soundly he will not feel any cutting." Arderne also used vinous mixtures of opium or hyoscyamus. He added the following warning, "And know that it is well to tweak the nose, to pinch the cheeks, or to pluck the beard of such a sleeper to quicken his spirits lest he sleep too deeply."[28]

The Renaissance saw the continued use of soporific sponges, for example, by Heinrich von Pfolspeundt, a Bavarian army surgeon in 1460.[21] Other oral potions containing hyoscyamus, opium, mandragora and a few other drugs were used by Hans von Gersdorff[20] and Hieronymus Brunschwig both German physicians living in 1497.[21] Mention is made by Jean Tagault a Frenchman in his *De chirurgiae institutione* of a local anesthetic composed of warm oil mixed with egg white or egg yolk to be applied to wounds to control the pain. He states that if the pain is severe oil of poppy, opium or mandragora is in order.[21]

By far the most important discovery in the field of anesthesia during the Renaissance was the discovery and subsequent synthesis of ether or "sweet

vitriol". Actually credit for the discovery of "sweet vitriol" should be given Ramondus Lullius of Spain who lived in the thirteenth century. Two centuries were to pass before the analgesic properties of this drug were to be recognized. Theophrastus Bombastus Paracelsus von Hohenheim rediscovered the "white fluid" while mixing sulfuric acid with alcohol, heating the mixture and condensing the steam. Trying this fluid upon chickens he made an observation which almost entitled him to be called the "founder of anesthesia."[8] "With respect to this particular vitriol, we must take a certain circumstance into account," he writes, describing his experiment. "Of all the extracts of vitriol this is the most important, being stable. Furthermore it has an agreeable taste, so that even chickens take it gladly, and thereafter fall asleep for a long time, awakening undamaged. In view of the effect of this vitriol, I think it especially noteworthy that its use may be recommended for painful illness and that it will mitigate the disagreeable complications of these."[25]

In 1540 Valerius Cordus (1515–1544) was the first to describe the synthesis of ether from sulfuric acid and alcohol. In his short life span of 29 years this remarkable man gave Europe its first pharmacopoeia; inaugurated the systemic study of botany and was a pioneer in the transition from alchemy to chemistry. The exactness of Cordus' methods showed he was a modern in chemical procedures. He noted several physical properties of ether, namely, its high volatility and the fact it was an excellent solvent for many substances not soluble in water. Cordus noted that medically ether could be used for "pleurisy, peripneumonia, and hacking cough to draw from the lungs pus and mucous."[28] Although used for these purposes for centuries after Cordus' discovery, ether was not used for anesthesia until March 1842 by Long.[19] The "sweet-vitriol" of Paracelsus and Cordus was named ether by the German apothecary Frobenius in 1792.[7]

Physical methods were employed for anesthesia during the Renaissance. Local anesthesia by compression of nerves was effected by Ambroise Paré in France in the sixteenth century. An account of regional anesthesia by compression of nerves and blood vessels of the region to be operated upon was used by the Italian, Valverdi in about 1600.[16] The Italians also produced an unconscious state for surgery by striking a wooden bowl placed on the head thereby producing a cerebral concussion.[6] In Italy also, the surgeon Severino in 1646 wrote of the use of freezing mixtures of snow and ice for surgical anesthesia.[16] It is reported that the employment of cold as a method of numbing sensation was not unknown among the very primitive peoples.

A number of references to anesthesia have appeared in the classic English literature. "In Brooke's *Tragicall Historye of Romeus and Julietta*, printed in 1562, which supplied Shakespeare with the plot and much material for his play *Romeo and Juliet*, Friar Laurence thus speaks to Julietta: 'I have learned and proved of a long time the composition of a certain paste which I make of divers somniferous simples, which heated afterwards to powdere, and dranke with a quantitie of water, within a quarter of an houre after, bringeth the receiver into such a sleepe, and burieth so deeply the senses and other spirits of life that the cunningest phistian will judge the party died. And besides that, it hath a more

marvellous effect, for the person which useth the same feelth no kind of grief and, according to the quantitie of the draught, the patient remaineth in a sweet sleepe; but when the operation is perfect and done, he returneth unto his first estate.'"[1] Shakespeare made several references to poppy, mandragora and other "drowsy syrups." The following is a quote from *Othello*. "Not poppy, nor mandragora, nor all the drowsy syrups of the world shall ever medicine thee to that sweet sleep which thou ow'dst yesterday."[5] The poet Marlowe also referred to the use of poppy and mandragora in his play "The Jew of Malta."

An interesting method of preparing an effective local anesthetic was employed by the Peruvian Incas. They chewed the leaves of the coca and the saliva which had dissolved the potent anesthetic component of the leaves was then applied to the part to be operated upon.[2] Successful trephinations using this form of anesthesia apparently were often performed.[19]

SUMMARY

In summary we see that man has for centuries sought victory over pain. The methods used were often violent, such as choking to produce unconsciousness by hypoxia, and the production of this state by striking a wooden bowl placed over the "victim's head" to cause a concussion. Man early sought more soothing methods of relieving pain. He turned to the herbs that grew out of the earth. The sedative and narcotic properties of the poppy, black hellebore, dittany, hemlock, lettuce, henbane, mulberry, hops and the root and apples of the mandragora plant were recognized by the ancient Greeks. Although the physicians and poets were familiar with the properties of these drugs it should not be assumed that they were used for surgical anesthesia. The Greek surgeons used wine for surgical anesthesia or no anesthesia at all as the dosage of these pain relieving drugs was altogether too uncertain to hazard their use for surgery. As we see by many of the accounts mysticism and ritual played a considerable part in the efforts to relieve pain by the ancients. Much doubt exists in the minds of readers of the veracity of many of these accounts, as for example the tale told of the Chinese physician Pien Ch'iao.

In the thousand years of the Middle Ages the contributions to man's search for effective pain relief were slight. Many of the drugs known and used in the Middle Ages were known also to the ancient Greeks. As the active principles (the alkaloids) of these drugs were unknown it was necessary to use the crude drugs. Similar quantities of identical appearing samples of drugs would produce a mild sleep in one patient and death in another. Although the sleeping sponge was used in this era it apparently could not have been too effective as the drugs used did not vaporize due to the fact that plant juices are not volatile. Drugged wine probably was the most effective narcotic besides being the safest and most convenient. Plenty of wine was used and just enough drug used so that it was sure not to be poisonous.

The Renaissance, although "the awakening" in the fields of art and science, made little contribution to the science of anesthesia. The discovery of ether was the only real effort of this era and its anesthetic powers were not utilized until

the eighteen-hundreds. Generally the potions used in the time of the Middle Ages continued to be used during the Renaissance. Most surgery was undertaken without benefit of anesthesia and the patient was strapped to the operating table or a chair. The "best surgeon" generally earned his reputation by being the "fastest surgeon". Alcohol was utilized as the most popular anodyne of the period and continued in this role until the use of ether which commenced in the eighteen hundred forties' by Long in 1842 and with Morton's demonstration at the Massachussetts General Hospital in 1846.

Thus we see that "anesthesia" prior to 1750 was a long stride behind modern surgical anesthesia as we know it today. The agents used were usually only partly effective in the relief of pain. Control and safety in administration were attributes the ancient anodynes lacked. For all the progress made in the field of anesthesia in these years a great deal more has been made in the 200 years after 1750. The anesthesiologist today is fortunate in having at his disposal many potent and versatile agents with which he can induce sleep and allay pain. In the future we may anticipate even more and better agents to be added to the anesthesiologist's armamentarium.

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EDITORIAL

VENA CAVA LIGATION: ADVANTAGES VS. DISADVANTAGES

Vena cava ligation so completely prevents pulmonary embolus formation arising from thrombosed areas in the veins of the legs and pelvis, that it should be the lone important procedure in the prevention of pulmonary embolus when these common sites are involved, and anticoagulant therapy is not considered to be feasible. Anticoagulants, valuable as they are, have not provided definite, permanent methods for this control. Technically, the operation is not difficult or dangerous in competent hands. Why, then, has not this operation received popular acclaim by the surgical profession? Perhaps weighing the benefits against the disadvantages attending the procedure could shed important light on the subject.

On the credit side, the operation is technically easy, and can be done through a safe retroperitoneal approach, unless it is desirable to ligate the ovarian veins in addition to the caval ligation. It is not a lengthy procedure; the immediate morbidity is slight; and the mortality is mainly due to the disease process and its degree of seriousness demanding the ligation. Shock and hemorrhage should not attend the operation unless there is a technical error.

The operation can be made permanent by dividing the cava, or temporary by placing a single catgut ligature following which recanalization will take place in the majority of patients. It can be employed safely even when the patient's condition is not the best. Suppurative peritonitis, intestinal obstruction or extensive tumors may be contraindicating associated conditions, but these rarely are present when the need of the ligation is actual. We have employed it successfully twice for thrombophlebitis cerulea dolens, and experimentally in ulcerated, doomed legs with extensive and old thrombophlebitis. There has been some improvement in the involved leg in the latter patients. Its virtue, however, remains in its ability to prevent pulmonary embolus. No one should hesitate to use the ligation for trauma, accidental or otherwise, when the hemorrhage cannot be stopped satisfactorily by simpler methods.

On the debit side, one can expect difficulties in the legs in approximately 66 per cent of the patients, and serious difficulties in approximately 34 per cent of the patients, according to our experience with the ligation in 33 male patients.

The sequelae consist of edema of the legs, ulcerations, weakness, and pain. These conditions must somehow arise from the increased venous pressure and the failure of the collateral veins, diseased or otherwise, to effectively provide an unimpeded return of venous blood in the extremities. The exact mechanism is not known. Various degrees of these complications denote the extent of the attending disability. Anticoagulant therapy and pressure bandages are said to be of great aid in avoiding these sequelae. Experience has shown that no postoperative regime, except bed rest with leg elevation, will absolutely control the edema, ulcerations, weakness and pain in some patients. There is no doubt that many

patients do not experience even edema, but it is difficult indeed to explain the fact that 1 patient demonstrates marked and disabling consequences and another will demonstrate practically none. The degree of existing disease in these leg veins is not the answer, because the complications may be most manifest when cava ligation is necessary for causes other than phlebothrombosis or thrombophlebitis. It also is a fact, from the study of our cases, that the leg uninvolved with recognizable disease tends to develop these severe complications with more regularity and extensiveness than its diseased twin.

If the edema is slight, temporary or transient, no significant disability exists. However, when the edema is marked, with thickened skin, pigmentation and ulceration, significant inconveniences are experienced by the patient. The postcaval ligation ulcer patients appear to suffer pain more than other stasis ulcer patients.

The existing confusion regarding the ligation is due to varying and absolutely contradictory observations, some of which follow:

I. A few reports minimize the sequelae almost to 0 per cent of significant involvement. Most reports include 30 to 40 per cent freedom from sequelae, but the remaining 60 to 70 per cent of the patients who develop edema and ulcers are regarded to be not important by some reporters, and extremely disabled by other reporters.

II. The edema and ulceration are regarded by some to be due to the disease process; by others to be the result of the ligation. The actual facts concerning these two views are not known. We have observed betterment of edema and ulceration in a thrombophlebitic leg when the opposite nonphlebitic leg became markedly involved after the ligation. Most reporters do not comment about this except to state that the uninvolved leg should not demonstrate significant sequelae.

III. It appears that caval ligation for pelvic suppuration in women, who demonstrate no leg vein involvement, is attended with less sequelae than in male patients who have thrombophlebitis and phlebothrombosis of both legs and pelvic veins. Perhaps these women do not possess the *diasthesis* for clotting seen in the other patients.

IV. The postoperative care creates confusion. Some advise bed rest with limited ambulation and leg elevation. Others advise two weeks' bed rest with leg elevation. Still others contend that early ambulation will prevent the complications. Almost all advise pressure bandages. Some use postoperative anticoagulants; others condemn their use. All, however, make comments about the ability of their postoperative measures to prevent the complications.

V. Very few unfavorable reports are published—a fact that is common in medical and surgical literature. In the case of vena cava ligation, this suggests to the writer that the majority of surgeons who have employed the procedure have seen a rate of frequency and extensiveness of disabling disease process so often, that they are extremely hesitant to use what should be a readily accepted operative procedure. What, then, prevents the employment of this operation, if not the appearance of these undesirable sequelae?

Vena cava ligation should certainly be employed for the prevention of pulmonary embolus when other methods, namely, anticoagulant therapy or lower ligation, do not or cannot safely control the embolizing effect of thrombosed areas in the legs or pelvis. It must not be lightly considered or employed, because disagreeable and disabling sequelae may result in 55 per cent to 70 per cent of the patients. There is no question that when competent, knowing observers judge the cava ligation to be a life-saving procedure, it must be employed promptly and without undue pessimism.

One wonders, then, why the cava ligation enthusiasts ever employ superficial femoral vein ligation, unless there is a contraindicative associated abdominal condition, or general or spinal anesthesia cannot be safely used. If ligation is regarded to be necessary, we would unhesitatingly employ vena cava ligation in all otherwise noncontraindicated patients if it were not for the appearance of these undesirable and frequently disabling sequelae.

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BOOK REVIEW

The editors of THE AMERICAN SURGEON *will at all times welcome new books in the field of surgery and will acknowledge their receipt in these pages. The Editors do not, however, agree to review all books that have been submitted without solicitation.*

Atlas of General Surgery. By JOSEPH R. WILDER, M.D., Assistant Professor of Surgery, The New York Medical College, New York City, New York. St. Louis, Missouri, The C. V. Mosby Company. Price $13.50.

There has been compressed in this Atlas an unusually large amount of information in regard to the technical procedures encountered by the General Surgeon. Its usefulness is quite obvious in that it makes possible a rapid study by both the busy surgeon and also the residents. The author has not entered into the controversial discussion as to the various merits of different procedures but emphasizes those that have proved most beneficial to him and to his group. Reasons for the various procedures are well documented by a tremendous amount of experience. The drawings are both anatomically and artistically well done. The detail with which the presentation is made affords little to be desired in a review of the various steps in any surgical procedure. The section on gallbladder has been well emphasized particularly the dangers encountered during gallbladder surgery and also measures for correction of the injuries which may have occurred on the biliary tract. This Atlas cannot be too highly recommended to all persons interested in surgery.

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